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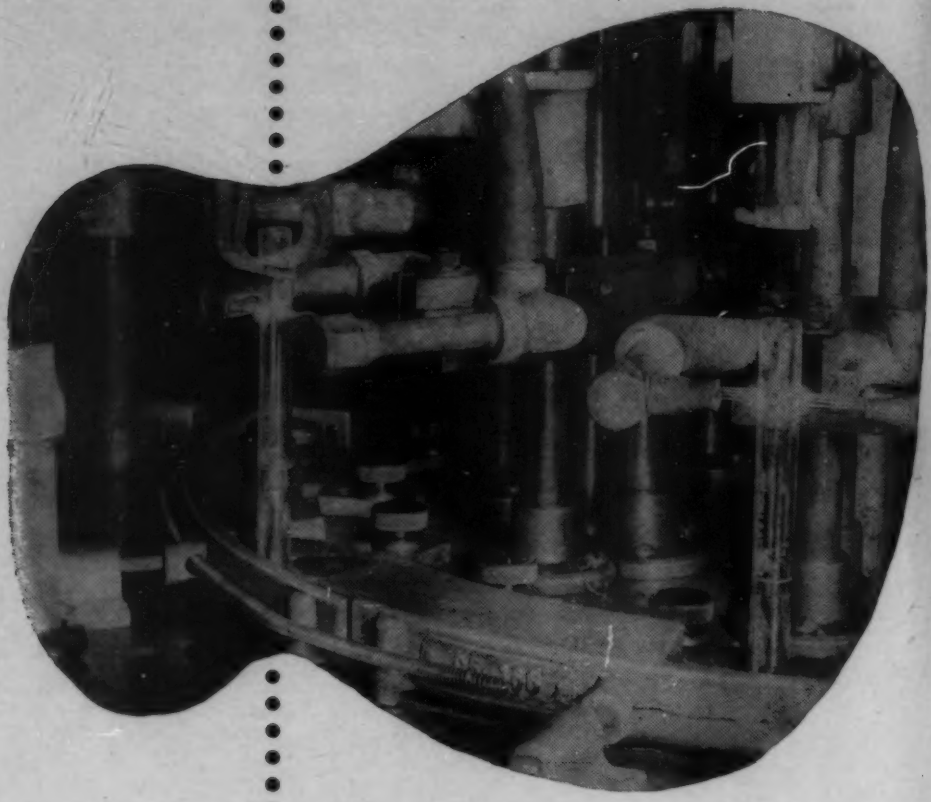

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The Journal of
Obstetrics and Gynaecology of the British Empire

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PLACENTA PRAEVIA

A Review of 200 Cases

BY

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IN the eight-year period from 1946–1953, 200 patients with placenta praevia were admitted to the Royal Maternity Hospital, Belfast. The management of these patients in the antenatal period and at delivery has followed closely the principles outlined by Macafee (1945) in his original paper which were based on experience gained in the personal supervision of a series of 174 cases. The treatment in the present series has been carried out, not by any one individual, but by various members of the consultant staff, obstetric tutors and registrars. In this way, an opportunity arises for strict evaluation of Macafee's principles of management; if the latter are sound they should be applicable by all experienced obstetricians with equally successful results.

CLINICAL GROUPING

The patients were grouped according to which of the following degrees or types of praevia were present:

First degree (Type 1). The greater part of the placenta lies in the upper segment of the uterus, only the lower edge of the placenta extending into the lower segment.

Second degree (Type 2). The lower edge of the placenta extends as far as the margin of the internal os. This degree is further sub-divided into Type 2 anterior and Type 2 posterior according to whether the placenta is attached mainly to the anterior or posterior uterine wall, these different locations having a bearing on the prognosis and on the method of treatment to be adopted.

Third degree (Type 3). The placenta completely covers the closed internal internal os but only partially so when the os is well dilated.

Fourth degree (Type 4). The lower uterine segment is covered almost completely by placenta.

In the clinical grouping of patients who were admitted with ante-partum haemorrhage, only those in whom the placenta was palpated in the lower uterine segment at vaginal examination, or noted to be implanted on the lower uterine segment at Caesarean section, were classified under the diagnosis of placenta praevia.

It must be admitted that this rigid standard of classification is far from satisfactory and this for two reasons:

(*a*) The possibility of excluding some cases of Type 1 placenta praevia. In the 8-year period under review, 34 patients each with a history of one or more episodes of painless vaginal haemorrhage in the later weeks of pregnancy were admitted to the hospital in labour; excessive bleeding was not present during labour, vaginal examination was therefore unnecessary and the mothers were delivered of 34 live infants *per vias naturales*. Examination of the placenta and membranes in each case was suggestive of Type 1 placenta praevia, and, although a high proportion of these cases undoubtedly were placenta praevia, they could not be included in the present series as the diagnosis had not been

confirmed accurately by vaginal examination. The exclusion of cases of this nature will lead to an unduly high proportion of major degrees of praevia in any series where the above standards of classification are adopted.

(*b*) The difficulty of making an accurate distinction between Type 3 and Type 4 praevia. This difficulty may be present even when the placental site is exposed at Caesarean section, and classification will then largely depend on the whim of the operator. In actual practice, the same treatment is employed for both degrees and much is to be said for combining them into one single group.

The numbers of the various types in the series are shown in Table I.

Onset of Haemorrhage

The average onset of bleeding was governed to a large extent by the degree of praevia, and ranged from the 34th week in the major types to the 37th week in the minor. In 27 cases haemorrhage occurred at or before the 30th week of pregnancy, and of these the placenta was Type 1 in 1, Type 2 anterior in 1, Type 2 posterior in 2, Type 3 in 14 and Type 4 in 9 patients.

Thirty-six patients merit special mention as they serve to illustrate a common and often dangerous feature, namely, that a placenta may be praevia, even of major degree, without giving rise to bleeding during pregnancy. In this type of case the diagnosis is made when there is severe bleeding at the onset of labour, at operation, or with more serious consequences at vaginal examination undertaken for some other obstetric complication, e.g., pre-eclamptic toxaemia prior to induction. In the 36 patients the placenta was Type 1 in 9, Type 2 anterior in 2, Type 2 posterior in 10, Type 3 in 9 and Type 4 in 6 patients.

Management

In the patients who were admitted at an early stage of pregnancy, for example, before 34 weeks, every effort was made to reduce foetal mortality from prematurity by prolonging the pregnancy to the 37th or 38th week provided this did not jeopardize the safety of the mother. This policy of expectant or conservative treatment was based on the realization that the initial haemorrhage in placenta praevia is seldom severe provided vaginal examination has not been carried out. In the present series, with the exception of 2 cases, bleeding either had ceased on arrival at hospital, or did so within a few hours after admission. The 2 cases mentioned illustrate the risk associated with vaginal examination; both had been examined at home and massive haemorrhage had resulted; on admission to hospital the patients were severely shocked and collapsed and required blood transfusion and operation; in each case bleeding was due to disturbance of a Type 4 placenta praevia and both infants were stillborn.

The length of time conservative treatment could be carried out with safety was determined mainly by the degree of praevia. In Types 3 and 4, repeated haemorrhages were common and often a sudden severe loss, following several small episodes or leading to a disturbance in the foetal heart rate, compelled operative interfer-

Table I

200 Cases	Primigravida 36	Multipara 164	
Stillbirths 10			
Neonatal Deaths 14			
Maternal Mortality .. .. Nil			

Type	Number	Average Onset of Haemorrhage	Per cent carried beyond or delivered after 36 weeks	Blood in pints
1	35	37 weeks	86·2	6
2 anterior ..	14	37 weeks	85·7	1
2 posterior ..	38	36½ weeks	89·5	8
3	66	34½ weeks	78·1	32
4	47	34 weeks	61·2	30

ence at an earlier stage than was desired. It must also be emphasized that many patients carried out their own expectant treatment at home until several episodes of bleeding finally forced them to seek medical advice.

During the period of waiting the patients' blood group and Rhesus factor were determined, the red cell count and haemoglobin level estimated at frequent intervals, and a speculum examination performed to exclude a local origin for haemorrhage. From 1952 soft tissue and displacement radiography to determine the placental site has been a routine investigation in all patients who are admitted with antepartum haemorrhage. The technique and results of this investigation in the diagnosis of placenta praevia in patients admitted to the Royal Maternity Hospital are shortly to be published. As a final investigation a "straight" X-ray is taken to exclude foetal abnormality. Seventy-five patients were treated by conservative measures and in this group the praevia was Type 1 in 4, Type 2 anterior in 3, Type 2 posterior in 13, Type 3 in 34 and Type 4 in 21 cases.

In patients who were admitted after the 37th week of pregnancy nothing was to be gained from further delay and treatment was deferred merely to determine the patient's blood group and to exclude foetal abnormality by X-ray. On completion of the investigations the patient was examined in the operating theatre, the diagnosis confirmed by vaginal examination and the treatment appropriate to the type of praevia instituted.

Methods of Treatment

The various methods of treatment employed in the different degrees of praevia are shown in Table II.

Type 1. In the earlier years of the period under review patients with Type 1 praevia were treated by artificial rupture of the membranes once the foetus was considered sufficiently mature to permit survival. In later years it has been the policy once diagnosis has been confirmed by vaginal examination to allow the patient to come into labour spontaneously and to reserve artificial rupture of the membranes for those patients who have more than a minimal loss of blood during labour.

It will be noted that 13 of the 35 patients with Type 1 praevia were treated by lower uterine segment Caesarean section. This high figure requires explanation; in 4 cases operation was undertaken for disproportion, in 4 for severe toxaemia, in 3 for prolapsed cord through a poorly dilated cervix, and in 1 on account of a history of difficult confinements; in the remaining case moderate bleeding persisted after artificial rupture of the membranes and foetal distress became manifest.

Type 2 anterior. Although artificial rupture of the membranes usually is sufficient to control haemorrhage in this degree of praevia, it will be noted that no less than 10 of the 14 patients were treated by Caesarean section. This high operative figure again demands explanation; operation was performed for disproportion in 2 cases, for diabetes in 2, for severe toxaemia in 1, for persistent transverse lie in 1, for prolapsed cord in 1, for poor obstetric history in 1, and on account of successful vaginal repair for stress incontinence in 1 case. In the remaining case foetal distress followed artificial rupture of the membranes. In 2 of the 10 patients there was no history of vaginal bleeding during pregnancy and the placenta praevia was diagnosed for the first time at operation.

Table II

Treatment	Type 1	Type 2 anterior	Type 2 posterior	Type 3	Type 4	Per Cent of Total
Nil	8	1	1	—	—	5·0
Artificial rupture of membranes	13	2	11	—	—	13·0
Artificial rupture of membranes and Willett's forceps	1	—	—	2	—	1·5
Version	—	1	3	5	—	4·5
Classical section	—	2	1	7	6	8·0
Lower uterine section	13	8	22	52	41	68·0

Type 2 posterior. Treatment and method of delivery in this degree were governed by the findings on vaginal examination. If the foetal head was engaged in the pelvis, or could be made to engage, artificial rupture of the membranes was the treatment of choice. Thereafter a frequent check was kept on the foetal heart for warning of compression by the foetal head of an umbilical cord inserted at the lower edge of the placenta. This complication occurred in 2 cases both of whom were delivered by Caesarean section immediately foetal distress was noted. In patients where the foetal head was above the pelvic brim and could not be made to engage, Caesarean section was performed. Version was undertaken in 3 cases where the infant was dead or considered too premature to survive. Of the various types of praevia, Type 2 posterior was the most difficult to treat and demanded considerable experience and judgment.

Types 3 and 4. All cases of Type 4 and the majority of Type 3 were treated by Caesarean section, either classical or lower segment. In the Type 3 group artificial rupture of the membranes and application of Willett's forceps was employed in 2 patients, and version in 5 where the baby was dead or unduly premature.

Blood Transfusion

The total amount of blood used before, during and after delivery was 77 pints, or less than a third of a pint per patient (Table I). Transfusion rarely was required during the antenatal period and even 3 or 4 episodes of bleeding were usually of small amount and not sufficient to lower the haemoglobin level to a dangerous degree. The majority of transfusions were given during Caesarean section in patients with Types 3 and 4 praevia when excessive bleeding frequently occurred. As a rule the bleeding originated in the large venous sinuses in the uterine wall or in the placental bed. A third uncommon but much more serious and alarming cause of haemorrhage was due to partial adherence of the placenta to the lower uterine segment rendering its complete separation and removal an extremely difficult undertaking. This hazard was encountered in 3 patients, 2 with Type 3 and 1 with Type 4 praevia; in each case the blood loss was considerable, 1 patient requiring 8 pints and the others 4 pints of blood during and after operation.

Results of Treatment

In the series, 201 infants were delivered and of these 10 were stillborn and 14 died in the neonatal period resulting in a gross foetal mortality of 11·9 per cent. One stillbirth due to hydrops foetalis was eliminated giving a corrected foetal mortality of 11·3 per cent. Two stillbirths were due to foetal abnormality, namely, anencephaly and hydrocephaly, but in view of the well recognized association of placenta praevia and foetal malformation, these infants were not eliminated. The maternal mortality was nil.

As previously stated, 75 patients (37·5 per cent) were treated by conservative measures for periods varying from 2–10 weeks; in this group there were 2 stillbirths and 6 neonatal deaths, giving a foetal loss of 16 per cent—a remarkably low figure when it is considered that 86·6 per cent of the 75 patients had a major degree of praevia, often with bleeding at an early stage in pregnancy.

The results of the various methods of treatment and the details of the stillbirths and neonatal deaths are set out in Tables III and IV. Apart from the 3 stillbirths associated with gross foetal abnormality, 3 infants were dead on admission to hospital, 2 died from intra-partum asphyxia and 1 from exsanguination following tearing of a vasa praevia at artificial rupture of the membranes. In the remaining case, internal version of a 7 pounds 8 ounces baby was carried out in a patient with a Type 2 posterior praevia —a gross error in judgment.

In the neonatal group, 4 of the 11 premature babies who were delivered by Caesarean section died from atelectasis. This is a disappointingly high proportion and serves to show one of the main hazards to the premature infant when delivered by this method.

Severe anaemia and foetal death from blood loss as a result of incision into an anteriorly situated placenta during lower uterine segment Caesarean section have been noted by several observers. Butler and Martin (1954), in a series

TABLE III

Results of the Various Methods of Treatment

Treatment	Number of Cases	Stillbirths	Neonatal Deaths	Percentage of foetal loss
Nil	10	1	1	8·3
Artificial rupture of membranes	26	1	—	4·2
Artificial rupture of membranes and Willett's forceps	3	—	1	4·2
Version	9	5	—	20·8
Classical section	16	2	2	16·7
Lower uterine section	136	1	10	45·8

TABLE IV

Type	Stillbirths	Neonatal Deaths
1	Normal delivery; intra-partum death. 5 pounds 6 ounces. Intra-uterine asphyxia.	—
2 anterior ..	—	L.U.S.C.S. at 38 weeks, 3 pounds 14 ounces. Died 11 hours later. Atelectasis.
2 posterior ..	Version. Baby dead on admission. Macerated. Hydrops foetalis.	Normal delivery at 37 weeks. 4 pounds 2 ounces. Died 6 hours later. Prematurity.
	Version. Intra-partum death. 7 pounds 8 ounces. Intra-uterine asphyxia.	—
	Version. Baby dead on admission. Hydrocephaly.	—
	A.R.M. Death from exsanguination due to ruptured vasa praevia. 7 pounds 7 ounces.	—
3	Version. 4 pounds 3 ounces. Anencephaly.	Classical Caesarean section at 40 weeks. 4 pounds 11 ounces. Died 8 hours later. Atelectasis.
	Version. 3 pounds 8 ounces. Intra-partum asphyxia.	L.U.S.C.S. at 34 weeks. 5 pounds 4 ounces. Died 8 hours later. Atelectasis.
	—	L.U.S.C.S. at 36 weeks. 6 pounds 2 ounces. Died 36 hours later. Atelectasis.
	—	L.U.S.C.S. at 30 weeks. 4 pounds 12 ounces. Prematurity.
	—	L.U.S.C.S. at 38 weeks. 3 pounds 12 ounces. Prematurity.
	—	Spontaneous onset of labour at 31 weeks. Application of Willett's forceps. 4 pounds 9 ounces. Prematurity.
4	C.C.S. at 36 weeks. Baby dead on admission. 10 pounds 1 ounce.	C.C.S. at 32 weeks. 4 pounds 4 ounces. Died 24 hours later. Prematurity.
	C.C.S. at 34 weeks. Patient collapsed on admission and foetal heart not heard. 5 pounds 8 ounces.	L.U.S.C.S. at 32 weeks. 4 pounds 12 ounces. Died 24 hours later. Prematurity.
	L.U.S.C.S. at 32 weeks. Patient collapsed on admission. Foetal heart not heard. 4 pounds.	L.U.S.C.S. at 39 weeks. 5 pounds 3 ounces. Died 48 hours later. Atelectasis.
	—	L.U.S.C.S. at 34 weeks. 5 pounds 4 ounces. Died 3 hours later. Intracranial haemorrhage.
	—	L.U.S.C.S. at 31 weeks. 4 pounds 3 ounces. Died 12 hours later. Prematurity.
	—	L.U.S.C.S. at 28 weeks. 2 pounds 4 ounces. Died 4 hours later. Intracranial haemorrhage.

of 19 cases where the placenta was incised, found anaemia in 5 infants, 3 of whom required transfusion. Neligan and Russell (1955) also stress the high incidence of foetal anaemia in cases of this type; in their series of 20 patients, no less than 7 infants required transfusion. In the Royal Maternity Hospital series, although incision of the placenta was a frequent occurrence foetal anaemia was not noted. Stab incision into the lower uterine segment, protection of the placenta by the forefinger while extending the incision and rapid delivery of the infant will do much to prevent blood loss from the foetal circulation.

Discussion

From 1932 the results in three series of cases of placenta praevia admitted to the Royal Maternity Hospital have been reviewed.

In the first series 76 patients were delivered between the years 1932 and 1936 with a maternal mortality of 2·6 per cent and a foetal mortality of 51·3 per cent. This high foetal mortality rate was in keeping with corresponding figures published from other centres and was attributed to two main causes (*a*) prematurity, the direct result of the concept that placenta praevia constituted an obstetric emergency which demanded immediate intervention, and (*b*) the methods of delivery, e.g., version, Willett's forceps, then employed.

The second series which may be regarded as a "test" series was that published by Macafee and comprised 174 cases delivered between the years 1937 and 1944 with a maternal mortality of 0·57 per cent, and a foetal loss of 23·5 per cent. Many valuable lessons were gained in the supervision of these patients and it was hoped that their future application would lead to a still further reduction in mortality.

The present, or third series, has realized this hope and it remains only to discuss briefly the five factors which have contributed so much to the results.

The first factor has been the very great help given by the general practitioners and midwives. With the exception of 2 patients the remaining 198 were admitted without a vaginal examination having been performed. Such cooperation and foresight have played a major role in the improved maternal and foetal mortality figures recorded. It is disturbing indeed to note that Mills of Birmingham and Snaith of Newcastle as late as 1951 complain of the high frequency of this examination by practitioners in their areas. The danger cannot be over-emphasized; in Qureshi's (1953) series of 200 cases, 30 mothers died and of these no less than 24 had been examined vaginally before admission. Accurate diagnosis may be satisfying to the practitioner but it will assuredly weigh heavily against the mother and infant.

The second factor has been the policy of conservative treatment in those cases where the infant was unduly premature to permit delivery. Conservatism was one of the two broad principles of management which evolved from Macafee's test series. In the series reviewed above it was carried out in 37·5 per cent of patients with a foetal loss of 16 per cent, whereas in 1,353 patients collected from reports of 24 hospitals in Great Britain and Eire it is interesting to note that only 13·5 per cent were treated conservatively for a period of 2 or more weeks and this with a foetal mortality of 24·5 per cent. Is the time-honoured dictum of Jaggard—"there is no place for the expectant treatment of placenta praevia"—undergoing a slow and lingering death or simply has a small recurrence of bleeding precipitated hasty and ill-timed interference?

The third factor and the other broad principle evolved from the "test" series has been the extended use of Caesarean section for delivery, especially in those patients with major degrees of praevia. The advantages of Caesarean section to mother and child and the hazards associated with the older methods of version, Willett's forceps and vaginal packing, were stressed by Macafee in his original publication and are sufficiently recognized not to require further elaboration.

The fourth factor has been the great improvement in the blood transfusion service. The value of readily available blood in the resuscitation of maternal collapse due to severe haemorrhage is obvious. Without blood being at hand vaginal examination should never be attempted in any case of suspected placenta praevia.

The fifth and final factor has been the very great help afforded by the paediatric service. Many infants are premature and demand specialized care and attention—in the series reviewed no less than 48 infants were under 5 pounds 8 ounces in weight and of these 13, or 25·4 per cent, died in the neonatal period. When it is recalled that 11 of the 13 infants were delivered by Caesarean section with its increased hazard to the premature baby, this is a remarkably low foetal loss.

Acknowledgments

I wish to thank Professor C. H. G. Macafee for his very great help and encouragement and for permission to use figures which he has collected from the reports of 24 hospitals in Great Britain and Eire. I am also grateful to the members of the Consulting Staff of the Hospital for access to the records of patients under their supervision.

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THE CONSERVATIVE MANAGEMENT OF THE SEVERE TOXAEMIC PATIENT

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THE management of patients with late pregnancy toxaemia is always a source of anxiety, especially during labour. Carey (1954) states that "if improved methods of inducing labour could reduce the failure rate to insignificant figures, if the dangers of infection of mother and foetus were practically eliminated, if rapid deterioration of toxaemic cases could be prevented and placental efficiency maintained, the indications for abdominal delivery especially of first babies would be materially reduced".

The use of an intravenous pitocin drip as recommended by Faris and Kahlenberg (1954) has proved highly successful, while Mauzy and Donnelly (1952) have also described a method of inducing premature labour by means of pitocin in women with toxaemia of pregnancy. The danger of infection has largely been reduced by the prophylactic use of wide-spectrum antibiotics. Thus two of the above objectives have been achieved to a great extent.

It occurred to the writers that, if some means of reducing the blood pressure during labour could be devised, conservative treatment of toxaemic mothers could be made a relatively safe procedure, as the dual dangers of placental insufficiency and eclampsia are considerably lessened when the blood pressure is kept within normal limits.

Huber (1951) has shown that premature infants delivered by Caesarean section have less chance of survival than those delivered by the vaginal route, yet frequently because of the severity of the toxaemia there is no alternative but to perform Caesarean section, for it is better to put a scar in the uterus than that the woman should get an eclamptic fit.

Thus it would seem that the choice between abdominal and vaginal delivery depends on two main factors: (*a*) the ease of induction of labour and (*b*) the control of toxaemia during labour. The writers believe that labour can be successfully induced by the use of intravenous pitocin combined with later puncture of the membranes when the cervix has been prepared. One of the main advantages of the pitocin drip is in cases of the unfavourable cervix several weeks from term. It appears to "prepare" the patient for surgical induction with a reasonable chance of success and so reduce the rate of Caesarean section in the termination of pregnancy in these cases.

They also believe that toxaemia can be controlled during labour, whether the patient be before or at term, by the use of hexamethonium bromide. In 1950–51 hexamethonium bromide was used at the National Maternity Hospital in women with non-convulsive toxaemia as a means of preventing the dreaded convulsion. A test dose of 10 mg. was injected intramuscularly and subsequent dosage governed by the response. Injections were given every 2 hours gradually increasing the individual dose to 100 mg. If the fall in blood pressure was too great, it was counteracted by methedrine and Trendelenburg's position, while if the response was insufficient the head of the bed was elevated. This method was found to be

reasonably satisfactory, but it was thought that the blood pressure fluctuated too much; and it was impossible to guarantee that sharp rises might not occur with possible onset of a fit before the next dose was due.

In 1952, at the suggestion of one of the writers (M. B. Quane), it was decided to attempt continuous administration of hexamethonium with a view to obtaining a more constant control of the blood pressure during labour.

The technique evolved is as follows: A test dose of 10 mg. of hexamethonium is given intramuscularly and the effect on the blood pressure in the horizontal position is noted. Then 200 mg. of hexamethonium bromide is dissolved in a pint of 5 per cent dextrose to which 10 units of hyaluronidase is added. A submammary drip is then set up, the hyalase promoting smooth absorption of the infusion fluid which is allowed to run in at 24 drops per minute. A sphygmomanometer is placed on the patient's arm and left in position to facilitate frequent observations of the blood pressure with the minimum of disturbance to the patient. The rate of administration can be regulated depending on the response of the blood pressure. In some instances the test dose alone will be sufficient to control the blood pressure at a safe level (Case 9).

The following are details of 12 patients in whom this method was used. As will be seen, they were all severe toxaemias for whom many obstetricians would have recommended Caesarean section as the treatment of choice. They were all delivered vaginally, none of them developed eclampsia, and only one baby was lost due to accidental haemorrhage following sudden rupture of the membranes in a case of hydramnios.

Case No. 1

This patient was aged 24 years and a primigravida.

Obstetrical history: This was normal until the 39th week when slight widespread oedema and hypertension appeared. There was no albuminuria. She was admitted at term because of failure of the toxaemia to respond to out-patient treatment. On admission the blood pressure was 150/90 and there was moderate widespread oedema with albuminuria+1 present. The vertex was presenting and the head was engaged. Complete bed rest and sedation with phenobarbitone failed to bring about any improvement. Four days later the forewaters were ruptured through an undilated cervix and medicinal induction given. Labour commenced 13 hours later. The blood pressure was now 170/110 and the albumen had increased to +2. She complained of severe headache, but had no visual disturbance. Treatment with submammary hexamethonium drip was then started. She was sedated with phenobarbitone gr. iii, pethidine mg. 100 and morphine gr. ¼ during labour. The behaviour of the blood pressure is shown by accompanying figures. At 9.10 p.m. she had a spontaneous delivery of a living infant weighing 6 pounds 6 ounces. The puerperium was uneventful. Her blood pressure on discharge was 170/120, at 8 weeks 150/110 and at 4 months 110/60.

Time	Blood Pressure	Hexamethonium Drops per Minute
2.35 p.m.	170/110	40
3.40 p.m.	110/70	40
3.55 p.m.	130/80	20
5.0 p.m.	140/90	20
6.30 p.m.	150/110	30
7.0 p.m.	180/140	90
7.30 p.m.	160/110	50
8.10 p.m.	120/90	20

Case No. 2

This patient was a primigravida, aged 18 years. She was an emergency admission at term having been 14 hours in labour before arrival. She had received no antenatal care. On examination there was widespread oedema which had been present for 2 weeks, her blood pressure was 180/100 and the urine showed +3 albuminuria. The vertex was deeply engaged and the cervix was 2-fingers dilated. She was sedated with pethidine mg. 100. A test dose of hexamethonium bromide mg. 10 had no effect on the blood pressure so a submammary drip was begun. Her hypertension then subsided and remained between 150 and 120 systolic for the remaining 6 hours of labour. Morphine gr. ¼ was given when the cervix was 3-fingers dilated. She was delivered of a normal living infant by easy low forceps extraction. The 3rd stage was normal. Her blood pressure ranged from 140/80 to 145/85 throughout the puerperium.

Case No. 3

This patient was aged 34 years, and had 2 previous full-time normal deliveries both alive and well. She was unbooked. She was admitted 19 days from term with a history from her own doctor of increasing albuminuria for 3 days. On examination her blood pressure was 210/120, albuminuria+2 and slight generalized oedema. She complained of headache and visual disturbances. Although sedated heavily for 24 hours there was no improvement. Surgical induction by puncture of the membranes was carried out and labour began 7 hours later. She had a spontaneous delivery of a normal infant weighing 7 pounds 5 ounces after a short labour of 2

hours. In all she was given 210 mg. of hexamethonium in 3 hours. Morphine gr. ¼ was given at the onset of labour. Her blood pressure on the first day of the puerperium was 180/105 and there was albuminuria+1, on the 9th day 220/110, and on discharge (12th day) 200/110 and albumen a trace.

Time	Blood Pressure	Hexamethonium Bromide
6.20 p.m. ..	190/120	10 mg. I.M.I.
6.30 p.m. ..	180/120	30 drops per minute
7.0 p.m. ..	180/120	60 drops per minute
7.15 p.m. ..	170/120	100 drops per minute
7.30 p.m. ..	170/110	120 drops per minute
8.0 p.m. ..	160/120	120 drops per minute

Case No. 4

This patient was a primigravida aged 37 years and unbooked. There was a family history of essential vascular hypertension. She was admitted at term in labour. Her blood pressure was 140/90, albuminuria+1 and she had slight oedema. The vertex was engaged and the cervix 3-fingers dilated. The membranes had ruptured. When the cervix was 4-fingers dilated, because her blood pressure rose to 180/110, a hexamethonium drip was started. Delivery was completed by low forceps extraction of a normal infant weighing 7 pounds 4 ounces. A total of 200 mg. of hexamethonium bromide was given. Her blood pressure on the 1st day of the puerperium was 130/80, albumen+1; on the 4th day 170/110, albumen nil; on the 9th day 170/110, albumen nil; and on discharge (14th day) it had fallen to 150/100.

Time	Blood Pressure	Hexamethonium Bromide
6.40 a.m. ..	180/110	10 mg. I.M.I.
6.45 a.m. ..	160/100	20 drops per minute
7.45 a.m. ..	170/100	40 drops per minute
8.30 a.m. ..	150/100	15 drops per minute
10.10 a.m. ..	140/105	15 drops per minute

Case No. 5

This patient, a primigravida aged 28 years, was booked. She was admitted at term because of sudden onset of toxaemia which had not manifested itself previously. On examination her blood pressure was 180/100. She had albuminuria+4 and generalized oedema. There were no subjective symptoms. Labour was induced by puncture of the membranes. A hexamethonium drip was commenced when the cervix was 2-fingers dilated. Her blood pressure at that time was 180/115. A total of 160 mg. of hexamethonium bromide was given over a period of 7½ hours. Delivery was completed by low forceps extraction of a living infant weighing 8 pounds 10 ounces. During labour she received pethidine 200 mg. and omnopon gr. ½.

Time	Blood Pressure	Hexamethonium Bromide
2.5 p.m. ..	170/120	10 mg. I.M.I.
3.0 p.m. ..	180/115	20 drops per minute
5.30 p.m. ..	155/95	36 drops per minute
7.30 p.m. ..	130/95	12 drops per minute
9.30 p.m. ..	130/90	20 drops per minute
10.15 p.m. ..	112/80	20 drops per minute

Case No. 6

This woman, a para-17, aged 43 years, was unbooked. All her previous deliveries had been spontaneous, but her 9th, 14th and 17th pregnancies had resulted in stillbirths due to combined toxic accidental haemorrhage. She was admitted at 34-weeks gestation in labour. There was marked hydramnios and the uterus corresponded in size with a pregnancy at term and was very tense. The cervix was 1-finger dilated and the foetal heart was heard. A vaginal examination to determine the presentation caused the membranes to rupture with the escape of approximately 4 pints of liquor amnii. The foetal heart could not now be heard. There was no revealed bleeding and her general condition remained good. The blood pressure was 200/110 and there was no albuminuria. A hexamethonium submammary drip was started shortly after admission and its effect on the blood pressure readings can be seen from the accompanying figures. After 15 hours in labour she had a spontaneous delivery of a stillborn infant weighing 4 pounds 9 ounces. The evidence of concealed haemorrhage was only present on completion of the 3rd stage when approximately half the placenta showed signs of premature separation. There were 15 ounces of old blood clot in the uterus where placental detachment had occurred following rupture of the hydramnion. During labour she was sedated with 200 mg. of pethidine, and a total dosage of 230 mg. of hexamethonium bromide was administered.

Time	Blood Pressure	Hexamethonium Bromide
12.55 p.m. ..	200/120	10 mg. I.M.I.
1.10 p.m. ..	200/110	20 drops per minute
1.30 p.m. ..	170/110	30 drops per minute
2.5 p.m. ..	160/100	30 drops per minute
3.0 p.m. ..	150/110	14 drops per minute
3.10 p.m. ..	140/90	14 drops per minute
5.25 p.m. ..	150/90	16 drops per minute
8.0 p.m. ..	120/80	16 drops per minute
10.30 p.m. ..	135/85	20 drops per minute
1.0 a.m. ..	140/80	16 drops per minute
2.30 a.m. ..	140/80	16 drops per minute
3.0 a.m. ..	140/90	16 drops per minute

Case No. 7

This woman was aged 38 years and a para-3. She was unbooked.

Obstetrical history: Her first pregnancy resulted in a full-time normal delivery, her second in a stillbirth at 38 weeks due to toxaemia, and her third in a full-time normal delivery.

Present pregnancy: She was admitted at 34 weeks because her blood pressure was 190/110 and she had +1 albuminuria. The breech was presenting and the foetal heart was heard. Twenty-four hours later her blood pressure was 210/105 and the lie of the foetus was now oblique. She was treated by puncture of the membranes combined with Braxton Hick's version. Labour commenced in 5 hours and a hexamethonium drip was begun. She was sedated with 100 mg. of pethidine during labour. The baby weighing 4 pounds 2 ounces was delivered by the breech without difficulty and thrived. Her blood pressure was 210/170 12 hours after delivery and 140/110 on the 10th day of the puerperium.

Time	Blood Pressure	Hexamethonium Bromide
11.50 a.m. ..	210/120	10 mg. I.M.I.
12.10 p.m. ..	185/120	24 drops per minute
1.20 p.m. ..	160/120	20 drops per minute
3.0 p.m. ..	160/110	24 drops per minute
5.0 p.m. ..	150/100	20 drops per minute
7.0 p.m. ..	160/110	20 drops per minute
9.40 p.m. ..	160/110	20 drops per minute

Case No. 8

This patient was 35 years of age and had attended for antenatal care.

Obstetrical history: On her first pregnancy she was delivered by lower segment Caesarean section for toxaemia; her second pregnancy resulted in an abortion; on the third she had eclampsia and was delivered by forceps of a stillborn baby; and on her fourth pregnancy she was again delivered with forceps of a living infant.

Present pregnancy: She first attended at 33 weeks. Her blood pressure was 135/90 and the urine was free of albumen. At 37 weeks her blood pressure was 160/90 and the urine showed albuminuria+2. Labour was then induced by puncture of the membranes, but the toxaemia increased during labour necessitating the use of hexamethonium. In view of the dramatic response to the test dose of hexamethonium only 100 mg. were introduced into the drip, and it can be seen that towards the end of the first stage of labour the dosage was inadequate. Delivery of a living baby weighing 8 pounds was spontaneous.

Time	Blood Pressure	Hexamethonium Bromide
4.0 a.m. ..	170/100	10 mg. I.M.I.
4.10 a.m. ..	110/70	None
4.20 a.m. ..	130/90	None
4.50 a.m. ..	130/100	None
9.45 a.m. ..	160/90	30 drops per minute
10.30 a.m. ..	220/110	30 drops per minute
11.0 a.m. ..	160/100	30 drops per minute
11.30 a.m. ..	150/100	30 drops per minute

Case No. 9

This patient, aged 30 years, was unbooked. Her first baby was delivered by forceps and weighed 9 pounds. On this pregnancy she was admitted at 38-weeks gestation because her blood pressure was 210/130 and she had albuminuria+3, with marked oedema. Labour was induced immediately by puncture of the membrane, and it lasted only 2 hours. Her blood pressure during labour was reduced from 180/130 to 140/110 by a single intramuscular injection of mg. of hexamethonium bromide.

Case No. 10

This patient attended regularly for antenatal care. She was aged 25 years and a primigravida. On admission she was well advanced in labour, the cervix being 3-fingers dilated; the membranes were unruptured. Her blood pressure was 160/110 and the urine showed +3 albuminuria. As labour progressed the toxaemia worsened. She was sedated with morphine gr. ¼ and pethidine 100 mg. during labour. A total of 210 mg. of hexamethonium bromide was administered. Delivery was accomplished by forceps, and the baby weighing 6 pounds 6 ounces was alive and well.

Time	Blood Pressure	Hexamethonium Bromide
10.0 p.m. ..	180/120	10 mg. I.M.I.
11.0 p.m. ..	140/90	40 drops per minute
12.0 p.m. ..	110/80	30 drops per minute
1.0 a.m. ..	130/90	40 drops per minute
1.30 a.m. ..	140/100	40 drops per minute

Case No. 11

This patient was 35 years of age. Her first baby was delivered spontaneously, but was premature and died at 2 weeks from gastroenteritis. She attended regularly for antenatal care in this pregnancy and was admitted at term in labour. Her blood pressure on admission was 180/115, her urine was clear and there was no oedema. The vertex was presenting and the cervix was 1-finger dilated. Three hours later her blood pressure was 180/120 and the urine showed a trace of albumen. A hexamethonium drip was set up which reduced the blood pressure to 160/110. Delivery was completed 3 hours later by an easy low forceps extraction. and during this time the blood pressure remained below 150 mm. systolic pressure. The baby weighed 6 pounds 12 ounces and was normal at birth. A total of 80 mg. of hexamethonium bromide was given during labour.

Case No. 12

This patient was aged 21 years and a primigravida. She attended regularly for antenatal care. On admission at term in labour the blood pressure was 150/100, there was slight widespread oedema and the urine showed a trace of albumen. When the cervix was 3-fingers dilated the blood pressure was 180/120 and she had +3

albuminuria. Hexamethonium bromide was given in a submammary drip following which the blood pressure fell to 140/100, at which level it remained for the duration of labour which lasted 3 hours. No alteration was noted in the albuminuria. The baby, alive and well, weighing 7 pounds 11 ounces, was delivered by low forceps.

The writers suggest that a review of this admittedly small series of cases demonstrates that fits can be prevented and placental complications diminished during labour in toxaemic mothers, and that the vaginal method of delivery can be selected in a large number with due regard for the safety of mother and child. Apart from the very gratifying falls in blood pressure, there is further proof that the hexamethonium bromide produces relaxation of arteriolar spasm in the immediate disappearance of headache and visual disturbances in all cases suffering from these symptoms. The writers are also satisfied from observation of many further cases not yet reported that urinary output improves when hypertension is reduced. Further, the combination of hexamethonium with chlorpromazine is still more remarkably potent in reducing blood pressure. Should post-partum haemorrhage occur in a case in which hexamethonium has been employed a speedy and complete restoration of blood loss is necessary just as has been found in surgical cases. This method has been employed at the National Maternity Hospital with complete satisfaction for the last 3 years.

The writers wish to acknowledge with sincere thanks the free supplies of Vegolysen received from Messrs. May & Baker, Ltd., for the treatment of these cases.

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THE PROBLEM OF THE TREATMENT OF PEPTIC ASPIRATION PNEUMONIA FOLLOWING OBSTETRIC ANAESTHESIA (MENDELSON'S SYNDROME)

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PARKER (1954) has recently drawn attention again to the danger of the inhalation of vomit in obstetric cases. We have seen 3 patients in which this has occurred with serious results and report them because of their practical importance and theoretical interest. Mendelson (1946) was the first one to draw attention to these cases and he distinguished two groups; the obstructive group due to the aspiration of solid food, and the asthmatic group due to the aspiration of fluid vomit. The second group is nearly exclusively found following anaesthesia in obstetrics and all 3 patients whom we report belong to this group.

Case 1. A primigravida, aged 34 years, attended the hospital antenatal clinic and her general health was satisfactory. A surgical induction when 41 weeks pregnant was carried out under anaesthesia because of postmaturity. The induction-delivery time was 115 hours. The labour lasted for 28 hours and, on account of poor uterine contractions, a low forceps delivery was carried out under cyclopropane and oxygen anaesthesia. A living female child was extracted and the third stage was normal. As the patient was regaining consciousness from the anaesthetic, vomiting occurred and this caused coughing. At first there was no cause for anxiety but 2½ hours after delivery the patient became desperately ill. There was marked cyanosis, dyspnoea and tachycardia. The pulse was almost imperceptible and the blood pressure was 80/60 mm. Hg. After a further 2 hours there was still deep cyanosis and marked dyspnoea. Extensive crepitations were heard at both lung bases and a tachycardia of 160/min. was present. The liver was palpable and tender. The E.C.G. showed sinus tachycardia and the radiograph of the chest (portable apparatus) showed patchy consolidation throughout the right lung fields and the left lingula (Fig. 1). Oxygen was administered and intravenous digoxin given. Four hours later the pulse rate was still 140/min. and the blood pressure 100/70 mm. Hg. The patient remained seriously ill for another 24 hours but made an uninterrupted recovery afterwards. Treatment consisted of penicillin and streptomycin, postural drainage and carbon dioxide inhalations.

Case 2. This patient, aged 37 years, attended the antenatal clinic and her health was satisfactory. There was a history of an abortion at 4 months, 1 year previously. A surgical induction of labour for postmaturity was carried out at 43 weeks. The induction–delivery time was 31 hours. After 24 hours in labour an easy forceps extraction was performed because the second stage contractions were of insufficient strength. The anaesthetic administered was nitrous oxide, oxygen and ether. A living male child was delivered, followed by a normal third stage. During the administration of the anaesthetic, vomiting occurred with inhalation of some fluid. A mechanical sucker to clear the air passages was used and the general condition of the patient at the end of the operation was satisfactory.

Three and a half hours after delivery sudden deterioration in the condition of the patient occurred; some cyanosis with extreme dyspnoea developed. The blood pressure was 85/55 mm. Hg. and the pulse was imperceptible. Oxygen was administered and a blood transfusion started. The total amount of blood given was 500 ml. After 1½ hours the patient was still deeply shocked and cyanosed with severe dyspnoea. There were extensive crepitations in both lungs. The pulse rate was 160/min. and the blood pressure 70/55 mm. Hg. In spite of the shocked condition the skin felt warm.

Treatment was now started with intramuscular cortisone 200 mg. Aureomycin and penicillin were also given. Approximately 3½ hours after the administration of the cortisone a marked improvement was evident. The blood pressure had risen to 130/80 mm. Hg and the pulse rate dropped to 130/min. A chest radiograph

showed extensive patchy consolidation throughout both lungs (Fig. 2). Recovery was uninterrupted and complete.

Case 3. A primigravida, aged 27 years, was admitted into hospital at term as an emergency case on account of pre-eclampsia. A surgical induction of labour was performed and the induction–delivery time was 95 hours. After 54 hours in the first stage of labour a lower segment Caesarean section was carried out on account of foetal distress. The anaesthetic administered was cyclopropane and oxygen. During the induction, vomiting occurred with inhalation of fluid. A mechanical sucker was used to clear the air passages and the anaesthesia then continued without further trouble. A relaxant (tubarine) was given. Further clearance of mucus from the air passages was carried out at the end of the operation. A living female child was delivered. The blood loss at operation was approximately 750 ml. and for this a blood transfusion (500 ml.) was given. The condition of the patient immediately following operation was satisfactory but 5½ hours later the patient became dyspnoeic and restless. The condition became worse with increasing cyanosis, thready pulse and a fall in blood pressure to 80/50 mm. Hg. Continuous oxygen was administered and a further blood transfusion (500 ml.) was given. In 1½ hours the patient's condition had only slightly improved with marked dyspnoea and moderate cyanosis still evident. There were extensive crepitations at both lung bases, the right being more involved than the left. The pulse rate was 150/min. and the blood pressure 75/50 mm. Hg. The skin was remarkably warm considering the shocked condition of the patient.

At this point, the treatment started was intravenous hydrocortisone (125 mg. in one litre of 5 per cent dextrose in 12 hours) and intramuscular cortisone 250 mg. In addition the patient had injections of penicillin and streptomycin. The condition commenced to improve rapidly and after 2 hours on cortisone therapy it was felt that there was no further cause for anxiety. After 4 hours the blood pressure was 105/75 mm. Hg. A chest radiograph (portable apparatus) showed patchy consolidation in the right middle and lower zones and an area of atelectasis in the right upper zone (Fig. 3). Recovery was uninterrupted and complete.

Discussion

Each of these cases shows a definite disease picture which, once it has been seen, cannot be mistaken. The history is characteristic. A surgical procedure is done to effect delivery and inhalation anaesthesia is used. Vomiting occurs during the operation but may be so slight as to be overlooked. Following the operation there is an interval from 2 to 5 hours when the patient's condition is satisfactory, then the onset of the illness is dramatic and the patient becomes extremely ill with cyanosis, dyspnoea and tachycardia. She presents a picture of acute pulmonary oedema. On examination the blood pressure is low and extensive crepitations are found at the lung bases. The skin is surprisingly warm considering the collapsed state of the patient. A radiograph of the chest shows patchy consolidation and the E.C.G. shows rapid sinus tachycardia.

Mendelson (1946) already has pointed out that this is a condition almost exclusively found in obstetric cases. We found it extremely hard to find a descriptive name for this syndrome which would describe all its main features. That is why we suggest that the name "Mendelson's Syndrome" should be adopted.

There is, however, one point in which our experience differs from Mendelson (1946), who considers that bronchospasm with asthma occurs in these cases. Parker (1954) also put great stress on the importance of generalized bronchospasm in such patients. In our cases no bronchospasm was found; there was no wheezing and the picture was rather that of pulmonary oedema. We have, therefore, considered the name "asthmatic type" a misnomer.

The incidence of these cases almost exclusively in obstetrics is surprising, since an emergency anaesthetic without any preparation of the patient is a much more frequent event in emergency surgery. Any tenable theory must explain this contrast. The explanation given by Parker (1954) that fluids are given to patients in labour is, in our opinion, insufficient. The same thing obviously applies to emergency and accident surgery. The explanation we offer is that the problem to be dealt with here is a state of acute adrenal insufficiency. This would explain the severe collapse and the extensive tissue reaction that is found in these cases. Also shock, together with a warm skin, has been described in the Waterhouse-Friderichsen syndrome. We have found the same sign in all our cases. The question why acute adrenal failure should affect the obstetric patient more than the surgical patient has to be considered.

It has been shown that the pituitary and the adrenal glands are peculiarly vulnerable during delivery. For example, the most frequent cause of pituitary insufficiency in the adult female is severe haemorrhage during delivery. Plotz (1953) has reported 56 cases, confirmed at post-

FIG. 1

Patchy consolidation throughout the right lung fields and in the left lingula.

FIG. 2

Lungs show areas of patchy consolidation on both sides, right more than left.

FIG. 3

Patchy consolidation in the right middle and lower zones. Area of atelectasis in the right upper zone.

W.H., R.L.L.

mortem, of severe adrenal damage in pregnancy. There is, however, another point which in our opinion is important and it is that the placenta is a most vital endocrine organ which produces considerable amounts of adrenocorticotrophic hormone and gluco-corticoids. Johnson and Haines (1952) have shown that human placental tissue extract has adrenal cortical hormone-like activity, although weight for weight to a lesser degree than adrenal tissue extract. De Courcy, Gray and Lunnon (1952) have shown the presence of cortisone and hydrocortisone by paper chromatography in placental tissue extracts. Even more convincing is the report by Jailer and Knowlton (1950) of a case of Addison's disease in pregnancy. They produce evidence that the adrenal cortex was non-functioning. Stimulation with A.C.T.H. 100 mg. daily for 5 days was followed by no increase in the 17-ketosteroid output or decrease in the eosinophil count. In spite of that fact, the excretion of neutral reducing lipids was normal in the last trimester and Thorn's test showed a 40 per cent fall of eosinophils 4 hours after the injection of 25 mg. A.C.T.H. To exclude the possibility that the foetal adrenal cortex was responsible, a 24-hour specimen of urine was collected from the newborn baby and this showed only approximately 5 per cent of the neutral reducing lipids compared with the mother's urine. The same authors also tested placental tissue extract for A.C.T.H.-like activity with positive results.

All this evidence suggests that the placenta in the late stages of pregnancy is an important endocrine organ and is at least partly responsible for the increase in A.C.T.H. and gluco-corticoids normally found in pregnancy. The sudden loss of this organ that occurs at delivery, will make it more difficult for the patient to meet a sudden increase in demand for gluco-corticoids when exposed to severe stress. To this must be added that involutional changes occur at this time in both adrenal and pituitary glands. It is, therefore, not surprising that a state of acute adrenal insufficiency may occur in these patients if exposed to severe stress. The stress in our cases was the aspiration of vomit and to that must be added the stress associated with the labour. Each patient had a surgical induction followed by an obstetrical operation to complete the delivery. In Case 3 pre-eclampsia was also present; Dewhurst (1951) suggested this as a possible factor in the production of suprarenal haemorrhage.

Unfortunately it was impossible for us to obtain laboratory evidence to prove our point. In any case such evidence is very difficult to procure and the diagnosis of acute adrenal failure has to be made on clinical evidence alone as Thorn (1954) has pointed out in his lecture on adrenal disease at the Royal Society of Medicine. Recently new methods have been introduced which measure hydrocortisone in the plasma and this procedure should put the diagnosis of acute adrenal failure on a firmer basis. We have tried the effect of cortisone treatment in 2 of our 3 cases and, although our results with this treatment were highly promising, they could not by the nature of things be convincing. We felt sure that the third case particularly, which was treated with intravenous hydrocortisone, did very much better than would have been expected without such treatment.

Treatment

All the steps necessary to prevent inhalation of vomit and the procedures that should be done if it occurs have been admirably described by Parker (1954). However, if the severe symptoms described above have developed, anti-spasmodics as suggested by Parker will be of little help. Intravenous hydrocortisone should be started immediately and 100 mg. should be given within 4 hours. Oxygen is obviously necessary and antibiotics, although necessary to prevent secondary infection, will have no effect on the immediate outcome as we have to deal not with an infection but with a chemical pneumonia.

Summary

Three cases of peptic aspiration syndrome following inhalation anaesthesia in obstetric patients are described. The hypothesis is advanced that these cases show acute adrenal failure and should be treated with intravenous hydrocortisone.

We would like to express our thanks to Mr. F. E. Wheeler and Mr. W. K. Frewen, Consultant Obstetricians to the Battle Hospital, Reading, for permission to record these cases; to Dr. E. H. P. Cave, Consultant Radiologist, Reading Combined Hospitals, for permission to publish the radiographs and to Dr. H. S. Le Marquand, Consultant Physician, Reading Combined Hospitals, for his help in preparing this paper, also to Miss E. Aust for photographing the radiographs.

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STUDIES IN PLACENTAL ACTION DURING PROLONGED AND DYSFUNCTIONAL LABOURS USING RADIOACTIVE SODIUM

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A PROLONGED first stage of labour due to uterine dysfunction still takes a heavy toll of foetal life, despite the introduction of new methods of treatment. Many of these stillbirths are attributable to intra-uterine asphyxia, arising from placental ischaemia. This latter condition is a frequent consequence of mechanical compression of the placental site and the maternal vessels which supply it, by the prolonged retraction of the uterus around the infant; a condition likely to be aggravated by early rupture of the membranes.

We have previously reported a considerable improvement in the foetal survival rate, when this type of case is managed by continuous caudal analgesia (Johnson, 1954). Quite apart from any direct influence the technique may have on uterine action, to accelerate the progress of labour, it seems likely that there may be a simultaneous vasodilatation effect in the uterine vessels supplying the maternal aspect of the placenta, similar to the concurrent dilatation of the lower limb vessels from the interruption of their vasomotor nerves.

We have, therefore, made a study of placental exchange in normal and prolonged labour, in order to decide whether a significant improvement in placental function is exhibited, when continuous caudal analgesia is employed in the management of a delayed first stage of labour.

Indices of placental action are calculated from the foetal uptake of normal saline which has been tagged with radioactive sodium, and administered to parturient patients in tracer doses. The comments and conclusions are based on 170 such measurements of placental action, in various types of labour.

The ability to trace minute quantities of radioactively labelled electrolytes in foetal tissues, following maternal administration just prior to delivery, suggests a ready method for studying the diffusion characteristics of the placenta in health and disease. This field of investigation was first explored in America by Flexner and Pohl (1941) and more recently by Cox and Chalmers (1953) and Browne and Veall (1953) in Great Britain. The former direct their attention to a quantitative assessment of placental action based on the total foetal uptake of radiosodium at delivery, and the latter to an antenatal assessment of placental action, calculated from the placental radiosodium clearance rates following intra-placental injection of radioactive sodium through the anterior wall of the uterus.

Conclusions as to placental action in this study are based on an analysis of the transfer rates of radiosodium across the placenta, as a function of the maternal plasma radiosodium in normal and abnormal cases, when 50 microcuries of Na^{24} have been administered to the mother by the intravenous route, a short while before delivery. The total radiation produced by this amount is less than 0·1 röntgen per day and that received by the foetus approximately 0·05 röntgen per day even assuming complete equilibrium between maternal and foetal circulations (Marinelli, Quimby and Hine, 1948). The short half-life of Na^{24}, of 15·0 hours, makes it particularly safe for foetal administration, since this property acts as a self-limiting mechanism

of any irradiation effect on the mother and child.

The physiological nature of normal saline, and the convenient physical properties of Na^{24} as an isotope with which to label it, has resulted in the majority of workers selecting this substance for placental studies. Na^{24} emits both beta and gamma rays, either of which can be used for measurement. Minute amounts of the former can be measured in fluids, such as plasma, using a liquid Geiger counter (Veall, 1948), whilst in deep tissues gamma rays can be detected by similar counters suitably disposed relative to the body.

Radiosodium techniques for placental assessment depend upon the assumption that the diffusion rates of sodium from mother to foetus reflect placental behaviour for essential foetal nutrients and metabolites. The justification for this assumption is demonstrated by the correlation shown to exist by other workers, between clinical assessments of placental efficiency and sodium transfer (Flexner and Pohl, 1941; Cox and Chalmers, 1953; Browne and Veall, 1953; Gellhorn *et al.*, 1943) which is further borne out by our own experience in the experiments to be described.

Discussion

If a small volume of isotonic saline labelled with Na^{24} is introduced into the vascular system it is distributed in the tissues in a complex way and at differing rates depending upon the organs and tissues into which it is diffusing.

In pregnancy there are additional complications due to the presence of the foetal sac, the increased plasma volume (Roscoe and Donaldson, 1946; Tysoe, Lowenstein and Simon, 1950) and increased extra-cellular fluid volume (Caton *et al.*, 1949).

After an interval of approximately 1 minute the introduced electrolyte attains equilibrium concentration within the maternal plasma and thereafter diffuses into the extra-cellular space (Fig. 1). This overall diffusion of sodium out of the maternal plasma involves a number of simultaneous processes taking place at differing rates (Kaltreider *et al.*, 1941; Burch, Reaser and Cronuch, 1947; Fauvert and Loverdo, 1950; Mannery and Bale, 1941). It has been suggested that these differing rates are due to the transfer into different fluid compartments of the body, and it has been possible to establish two major rates of sodium transfer for the non-pregnant human:

(1) A rapid diffusion process into the extra-cellular tissues of the muscles and viscera.
(2) A slower diffusion process into the tissues of the brain, central nervous system and bone.

It seems likely that the slow phase itself comprises a number of discrete diffusion rates and in particular identification has been made of sodium transfer to bone (Evans *et al.*, 1948) and enamel and dentine (Hodges *et al.*, 1943).

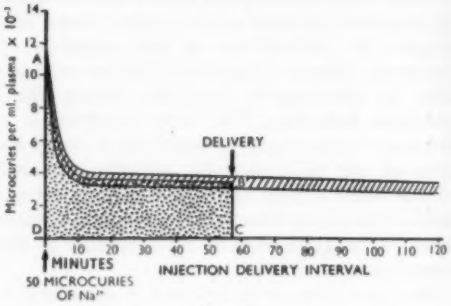


Fig. 2

Curve showing the overall maternal plasma diffusion rates of Na^{24}, in 18 normal pregnancies.

We have measured the diffusion rate of the fast phase (Fig. 2) and find a value in accord with that reported by Cox and Chalmers (1953). Equilibrium concentration in the extra-cellular space of the mother is reached approximately 10 minutes after the initial injection. We have not attempted to assess accurately the final maternal plasma concentration resulting from the slow phase, but it is significant that our observations, which were made up to 3 hours after the instant of injection, did not show equilibrium concentration between mother and infant.

In addition to the above there is also an exchange of radiosodium taking place within the foetus where it is probable that similar fast and slow diffusion processes are occurring.

There are, furthermore, other considerations

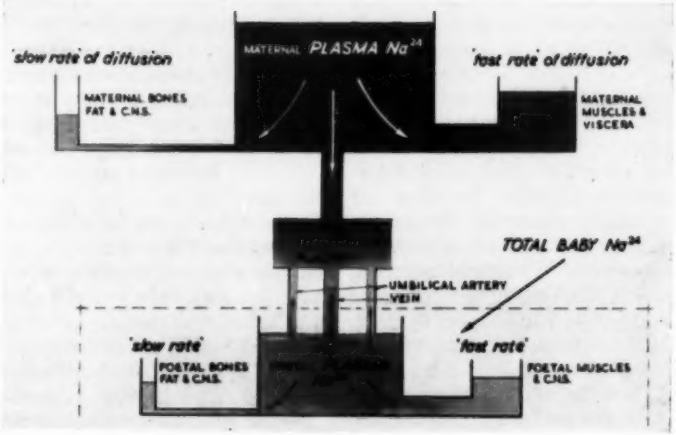


FIG. 1

Diagram representing the diffusion gradient of Na^{24} into maternal and foeta tissues, following maternal administration.

which to a greater or lesser degree affect placental function: or at least the assessment of it by measurement of isotope concentration. There are likely, for instance, to be variations in the weight of the placenta; in the area of placental villi bathed by maternal blood in the intervillus space; in the permeability of the villi to radiosodium and in the difference in concentration on either side of the diffusing membrane. The transfer rate of radiosodium across the placenta is also known to vary with the gestation period (Flexner *et al.*, 1948).

Each of the above considerations introduces a separate variable of differing significance and it is clear that the first requirement is to minimize their number so that a useful measurement of placental transfer rate can be made.

With this in mind we have restricted our observations to the period after equilibrium of Na^{24} was achieved in the maternal plasma so that from this point of view radiosodium plasma concentration was effectively constant.

In this treatment the placenta is regarded as a single membrane to which an overall figure of merit has been attributed. Variations in weight, for instance, though recorded have been ignored. This is in accordance with the work of Christofferson (1934) who showed that the effective placental area is independent of the volume or weight.

By restricting observations to patients delivered at term, variations in placental transfer rate with gestation period as reported by Gellhorn *et al.* (1943) have been overcome.

The ideal method of determining transfer rates would be to have direct access to the placenta and foetus, so enabling continuous measurement of the accumulation of Na^{24} to be made. It is unfortunate that the inaccessibility of foetus and placenta and the inability to predict precisely the termination of the second stage of labour prevents this and so restricts investigations to single observations made at delivery. It is, therefore, only by varying the injection delivery interval in a number of cases that it is possible to construct a curve showing the approach to equilibrium concentration in the foetus in normal cases.

From Fig. 1, which is a diagrammatic representation of the diffusion characteristics, it is clear that the radiosodium incident to the placental villi in the decidua basalis and available for foetal transfer is an ever diminishing quantity dependent upon the fast and slow diffusion rates. It is clear that a quantitative assessment of these is an essential prerequisite to any consideration of radiosodium concentration on either side of the placental membrane.

By making a simple numerical integration it is possible to allow for the diminishing maternal plasma sodium concentration so that assessment of the amount available for placental transfer can be made.

Two methods of establishing placental function have been adopted.

(1) The total quantity of radiosodium transferred to the foetus in a given time is related to the maternal radiosodium level, taking into account the diminishing plasma concentration in the decidua basalis. This method of assessing placental function is independent of diffusion characteristics of the foetal tissues and is thus a direct measure of the ability of the placenta to transfer sodium electrolyte. Total radiosodium as an index of placental function has been used by other workers (Flexner *et al.*, 1948) who have macerated the new born infant and extracted the radiosodium in solution. This technique has restricted certain previous experiments to animals and non-viable infants. We have overcome the difficulty by constructing a special cot surrounded by a ring of Geiger counters into which the baby is placed. By this means it has been possible to measure radiosodium accumulation in any new born child.

(2) The ratio of plasma radiosodium concentration in the umbilical vein to that in the maternal vein at the instant of delivery has also been used as a measure of placental transfer efficiency. The influence of the foetal–placental return has been considered but, in view of the nature of the placental circulation and the long foetal circulation time (Wendle, 1940), we regard this approach as justified and not likely to introduce any serious error.

It should be emphasized that the object of this study has been to measure the overall efficiency of the placenta in transferring radiosodium, and to correlate numerical results with clinical conditions.

Method and Results

(a) *Normal pregnancies and deliveries*

10 ml. of isotonic saline containing approximately 50μcs Na^{24} was injected into the anticubital vein of the mother at varying times between 2 minutes and 3 hours before delivery of the infant. Complete miscibility with the maternal blood was confirmed by placing a Geiger counter over the point of injection.

In 18 of 69 normal cases 5 ml. samples of blood were withdrawn at 2- to 10-minute intervals following the instant of injection. Each sample was obtained in a clean heparinized syringe and centrifuged immediately to prevent diffusion of radiosodium into the red cells. The centrifuged plasma was withdrawn using a separate micro-pipette for each sample. It was diluted to 10 ml. and assayed in an M6 Geiger counter (Veall, 1948) the chamber of which held exactly 10 ml. of liquid. The Geiger counter was connected to a scaler and the background counting rate was approximately 15 c. per minute.

To assay the plasma activity the mean of 3 counts was made, to give a statistical accuracy greater than ±1 per cent. All counts were corrected for radioactive decay and referred to the time of injection.

The counters used were calibrated daily against a standard radium source.

From these results the diffusion of radiosodium from the maternal plasma was determined. The general nature of this curve has previously been established (Cox and Chalmers, 1953; Flexner *et al.*, 1948; Gellhorn, Merrell and Rankin, 1944) and hence much of our work is of a confirmatory nature.

The results obtained from 18 cases are exhibited graphically in Fig. 2 which is in agreement with previous plasma diffusion curves reported by Flexner *et al.*, (1948) and Cox and Chalmers (1953). The numerical value of the area ABCD represents the total radiosodium available for placental transfer during an injection delivery interval of 58 minutes in a specific example of a patient having a plasma radiosodium concentration of $3{\cdot}5\times10^{-3}$μcs per ml. at the time of delivery.

The total quantity of radiosodium transferred to the foetus during the same injection delivery interval was measured directly by placing the new born infant in the special cot already mentioned. The length of the counters and their disposition was chosen so that accurate positioning of the baby in the cot was not necessary. A statistical accuracy of count of ±1 per cent was achieved in all cases.

The actual activity of radiosodium was derived by comparing the counting rate from each baby with that from an aliquot of the injected solution placed in the centre of the cot.

The placental transfer efficiency is expressed as the ratio of the total radiosodium in the baby to the total available radiosodium incident to the

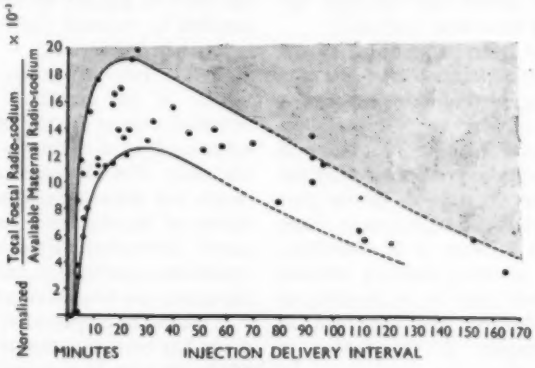


FIG. 3

Method 1. Curve of foetal accumulation of Na^{24} obtained from 42 normal pregnancies and deliveries.

maternal aspect of the placenta and calculated from the integral of the maternal plasma concentration curve between the times of injection and delivery (Fig. 2). The derived curve which is shown in Fig. 3 was constructed from measurements on 42 normal pregnancies and deliveries. It has a mean total deviation of approximately ±15 per cent.

The rise in the curve results from the rapid initial transfer of radiosodium whilst the maternal plasma radiosodium concentration is decreasing. The fall in the curve following the maximum at 25 minutes is due to the diminishing rate of transfer as the concentration gradient across the placenta is reduced while the integral value derived from the maternal radiosodium diffusion curve continues to increase.

In 56 normal cases samples of maternal blood were obtained only at delivery and were assayed for radioactivity concurrently with samples of plasma from the umbilical vein and artery obtained at the same time. The radioactive content was established by calibrating against an aliquot of the injected solution and placental function was expressed by the ratio of the radiosodium concentration in the foetal venous plasma to that in the maternal venous plasma.

The curve showing the approach to equilibrium concentration in the foetus is exhibited in Fig. 4. The mean total deviation is ±10 per cent.

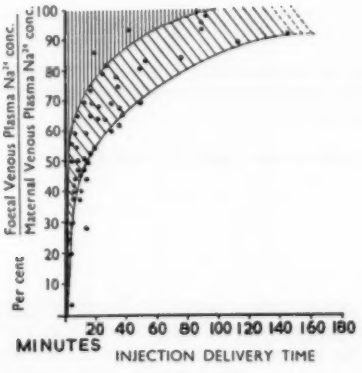


FIG. 4

Method 2. Curve of foetal accumulation of Na^{24} obtained from 56 normal pregnancies and deliveries.

(*b*) *Abnormal pregnancies and deliveries*

Having established a series of normal values of placental function it becomes a simple matter to investigate change in radiosodium transfer rate in any selected delivery in which there is clinical evidence of disturbed placental action as judged by the clinical state of the infant or its placenta post-partum.

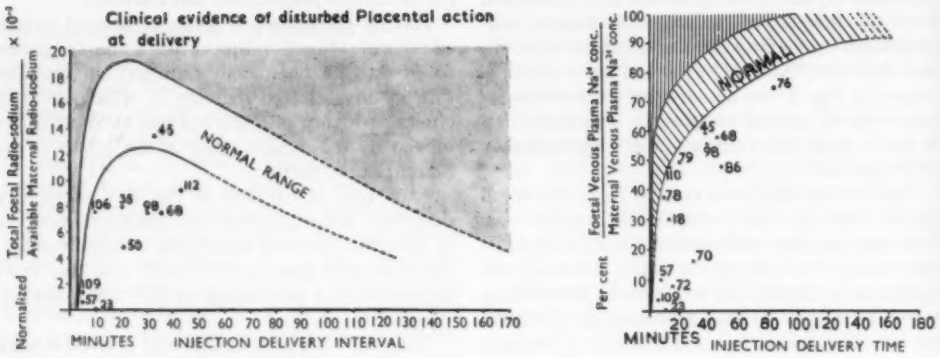
Each case is handled in the way previously described, and compared with the normal curves of placental function illustrated in Figs. 3 and 4. The placental function for each case has been expressed as a percentage of the mean normal range.

The following pregnancies and deliveries were investigated in the manner described, and the results are tabulated below.

(1) 18 cases exhibiting clinical evidence of disturbed placental action at delivery.
(2) 9 deliveries complicated by pre-eclampsia at this time.
(3) 9 prolonged and dysfunctional labours exceeding 48 hours in duration managed conservatively by sedation.
(4) 11 prolonged and dysfunctional labours, exceeding 48 hours in duration, conducted under continuous caudal analgesia.

Fig. 8 records the ratios observed in 11 cases of prolonged and dysfunctional labour conducted under continuous caudal analgesia, in the manner previously described (Johnson, 1954). The purpose of the technique is to accelerate the progress of labour, and simultaneously to induce a vasodilatation effect within the decidual vessels, by paralysing their sympathetic vasomotor nerves. The tendency for a larger number of points to fall nearer the normal range when this method is employed is apparent when compared with Fig. 7, in which 10 of the 12 points fall outside the normal limits. In the caudal group, only 3 out of 20 ratios fall outside these limits, 1 of which, number 46, refers to a breech delivery in which some degree of foetal asphyxia is inherent in the method of delivery.

Realizing the increased foetal hazard of a prolonged labour, when the membranes have been ruptured for a long time, we have examined our results to determine a possible relationship between loss of placental function, and duration of ruptured membranes. It would seem reason-


Clinical evidence of disturbed Placental action at delivery
Normalized Total Foetal Radio-sodium / Available Maternal Radio-sodium × 10⁻³
NORMAL RANGE
MINUTES INJECTION DELIVERY INTERVAL
Per cent Foetal Venous Plasma Na²⁴ conc. / Maternal Venous Plasma Na²⁴ conc.
NORMAL
MINUTES INJECTION DELIVERY TIME

Expt. No.	Clinical Features	Placental Function Percentage of Average Normal Method 1	Method 2
18	Prolapsed arm. Internal version	—	52
23	Ruptured uterus. Fresh stillbirth	Nil	Nil
35	Prolonged second stage of labour	48	—
45	Deep transverse arrest	80	76
50	Foetal distress. Forceps delivery	30	—
57	Fibrotic placenta. Neonatal death	11	20
68	Assisted breech delivery	46	73
70	Prolapsed cord. Internal version and breech extraction	—	23
72	Foetal distress	—	20
76	Accidental haemorrhage	—	76
78	Accidental haemorrhage	—	70
79	Ruptured vasa praevia	—	77
86	Obstructed labour. Caesarean section	—	53
98	Prolapsed arm. Caesarean section	46	70
106	Prolonged second stage of labour	53	—
109	Assisted breech delivery	11	15
110	Cord twisted round trunk	—	76
112	Obstructed labour. Caesarean section	52	—

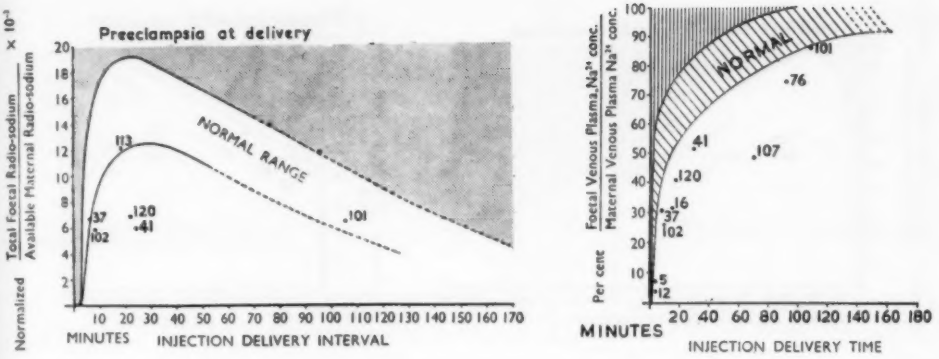
FIG. 5

Ratios for 18 examples of disturbed placental function superimposed upon the normal range.

able to anticipate such a relationship and, although we find some evidence in support of this, we have been unable to demonstrate this point conclusively. This is possibly due to the fact that placental ischaemia is inherent in a prolonged labour, and the added complication of ruptured membranes is not significantly discernible.

CONCLUSIONS

It has been found possible to establish a consistent series of values for placental transfer of


Preeclampsia at delivery
NORMAL RANGE
Normalized Total Foetal Radio-sodium / Available Maternal Radio-sodium × 10⁻³
MINUTES INJECTION DELIVERY INTERVAL
Foetal Venous Plasma Na²⁴ conc. / Maternal Venous Plasma Na²⁴ conc.
Per cent
NORMAL
MINUTES INJECTION DELIVERY TIME

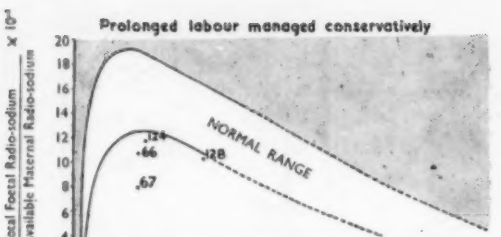
Expt. No.	Blood Pressure	Oedema	Albuminuria g./litre	Placental Function Percentage of Average Normal Method 1	Method 2
16	140/90	Generalized	½	—	53
37	180/100	—	½	58	62
41	200/110	Generalized	3	40	60
76	140/105	—	—	—	72
101	120/70	Limbs	—	85	90
102	140/90	—	½	48	47
107	160/100	—	½	100	58
113	150/100	Limbs	—	78	—
120	170/110	—	5	44	50

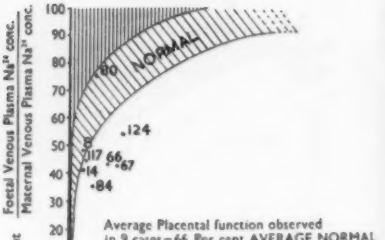
FIG. 6

Ratios for 9 examples of pre-eclampsia at the time of delivery, superimposed upon the normal range. It is of interest to note that the numerical value of placental function determined for each case bears a close relation to the severity of the condition.

radiosodium in 98 normal pregnancies and deliveries, and significantly low values have been demonstrated in labours complicated by placental ischaemia, for one reason or another.

In many cases of prolonged labour, there is a severe reduction of placental action, which in some cases may be as low as 50 per cent of the normal mean value. Interruption of the vasomotor nerve supply of the uterine vasculature by continuous caudal analgesia results in a demonstrable improvement in placental action, presumably from a direct vasodilatation effect on





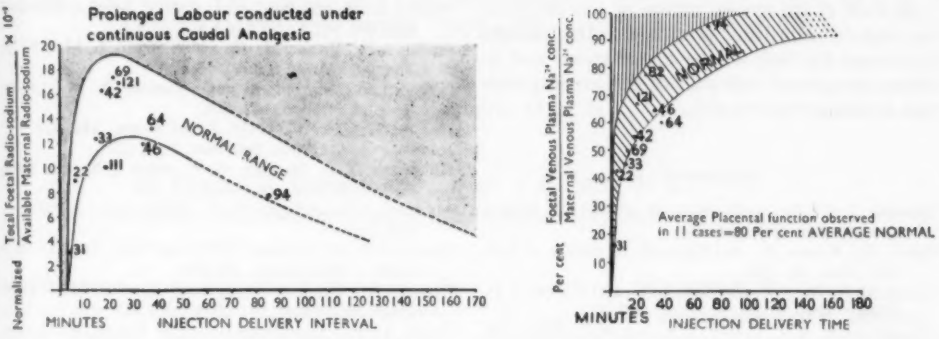
Expt. No.	Clinical features	Duration of ruptured membranes Hours	Total duration of labour Hours	Placental function percentage of average normal Method 1	Method 2
8	Hypotonic. Forceps delivery ..	8	67	—	83
14	Hypotonic. Forceps delivery ..	31	49	—	74
66	Hypotonic. Forceps delivery ..	1¼	59	66	55
67	Hypertonic. Forceps delivery ..	2	50	50	57
80	Hypotonic. Forceps delivery ..	2	53	—	103
84	Hypertonic. Forceps delivery ..	3	50	—	55
117	Hypotonic. Caesarean section	4	48	—	65
124	Hypotonic. Forceps delivery ..	22	48	71	70
128	Hypertonic. Caesarean section	65	62	66	—

FIG. 7

Ratios for 9 cases of prolonged labour managed by sedation, and intravenous fluids. Mean placental function=66 per cent of average normal.

the decidual vessels, akin to the original observations of Van Wagenen (1933), and the views previously expressed by Flexner that placental exchange may bear some relation to the blood-flow in the decidua basalis.

Our findings may appear contrary to the views expressed by Flexner and his colleagues, who conclude there is no evident difference in placental function when spinal or caudal analgesia are employed at delivery. Flexner's views, however, are based on normal labours, uncomplicated by a protracted first stage.


Prolonged Labour conducted under continuous Caudal Analgesia
Total Foetal Radio-sodium / Available Maternal Radio-sodium × 10⁴
Normalized
NORMAL RANGE
MINUTES
INJECTION DELIVERY INTERVAL
Foetal Venous Plasma Na²⁴ conc. / Maternal Venous Plasma Na²⁴ conc.
Per cent
NORMAL
Average Placental function observed in 11 cases=80 Per cent AVERAGE NORMAL
MINUTES
INJECTION DELIVERY TIME

Expt. No.	Clinical features	Duration of ruptured membranes Hours	Total duration of labour Hours	Placental function percentage of average normal Method 1	Method 2
22	Hypotonic. Forceps delivery ..	45	54	65	80
31	Hypotonic. Caesarean section..	44	52	48	30
33	Hypotonic. Forceps delivery ..	12	60	72	70
42	Hypotonic. Forceps delivery ..	16	60	89	83
46	Hypotonic. Breech extraction	50	58	68	84
64	Hypertonic. Forceps delivery ..	8	65	83	78
69	Hypotonic. Forceps delivery ..	28	58	109	81
82	Hypotonic. Forceps delivery ..	8	71½	—	100
94	Hypotonic. Caesarean section..	7½	55	71	106
111	Hypotonic. Forceps delivery ..	4	52	58	—
121	Hypotonic. Forceps delivery ..	9	73	105	95

FIG. 8

Ratios for 11 cases of prolonged labour conducted under continuous caudal analgesia. Mean placental function = 80 per cent of average normal.

We submit our conclusions as further justification for the therapeutic application of continuous caudal analgesia to complications of labour in which placental action is embarrassed, with special reference to a prolonged first stage of labour.

ACKNOWLEDGMENTS

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for the facilities provided by his department. This work was financed by a research grant from the Newcastle-upon-Tyne Regional Hospital Board.

In view of the special nature of this research, we wish to record our gratitude to the patients concerned for their willing cooperation, and to whom the general character of this investigation was explained beforehand.

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THE EFFECT OF THE HYDROGENATED ERGOTOXINE-GROUP ALKALOIDS ON THE INTACT HUMAN UTERUS

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IN attempts to overcome the dysrhythmia of contractility in cases of incoordinate uterine action in labour, sympatholytic drugs have had some vogue in recent years. The first drug used for this purpose was dihydroergotamine. This was claimed to be devoid of direct *oxytocic* properties, and was believed to shorten labour by hastening cervical dilatation through an adrenaline-blocking or *sympatholytic* mechanism (Sauter, 1948; Gill and Farrar, 1951; Baskin and Crealock, 1950, 1951). A few clinicians have, however, warned that the administration of dihydroergotamine is not without considerable risk, and the prodigious foetal mortality of 25 per cent has even been reported following its use (Altman *et al.*, 1952).

Recently, one of us showed that dihydroergotamine failed to impede the action of circulating adrenaline on the intact human uterus in labour (Garrett, 1955). As this finding invalidated the theories previously advanced regarding the mode of action of dihydroergotamine, further studies were undertaken in which we were able to demonstrate that, in reality, the drug exhibited simple, direct oxytocic properties. Qualitatively dihydroergotamine resembled the parent alkaloid ergotamine in every respect, although quantitatively it was somewhat weaker in action (Embrey and Garrett, 1955).

With this evidence before us it seemed appropriate that the newer semi-synthetic hydrogenated alkaloids related to ergotoxine should be investigated along similar lines to our earlier work.

"HYDERGINE"*

A mixture of dihydroergotoxine, dihydroergocristine and dihydroergokryptine, available under the trade-name "Hydergine" contains 0·3 mg. of the mixed methanesulphonates (0·1 mg. of each) per ml. of solution.

One constituent, dihydroergotoxine has also been known as dihydroergocornine but for this there seems little justification. The parent alkaloid ergotoxine was first described by Barger and Carr in 1906, although possibly in an incompletely pure form. It was later redescribed under the name of ergocornine by Stoll and Hofmann in 1943. As Foster (1945), Foster, Smith and Timmis (1946) and Henry (1949) have pointed out, it seems quite unnecessary to give a new name to a substance which has been known as ergotoxine in the chemical, pharmacological and clinical literature for almost 40 years. Accordingly, to indicate the relationship to the parent alkaloid, we prefer and shall use the name dihydroergotoxine, instead of dihydroergocornine, for the hydrogenated product.

Rothlin (1947) has stated that all three hydrogenated derivatives of the ergotoxine group fail to have an excitatory action on the rabbit uterus and, indeed, has recorded that they inhibit the "utero-tonic" effect of the natural alkaloids such as ergotamine. A similar lack of oxytocic activity in the rabbit has been ascribed to the mixture "Hydergine" by Berde and Rothlin (1953). However, these workers have not infrequently found some evidence of an oxytocic effect in the cat and, more recently, they have occasionally recorded direct stimula-

* Hydergine and its constituents used in this work were kindly supplied by Professor E. Rothlin of Basle, through Sandoz Products Ltd., London.

tion with strips of human myometrium obtained at Caesarean section (Rothlin and Berde, 1954). Interesting though they may be, such results bear little relationship to the actual response of the *intact* human uterus; the only reliable test of oxytocic activity is on the human puerperal uterus itself (Gaddum, 1953).

Strong sympatholytic properties have been ascribed to each of the constituent alkaloids of Hydergine when tested on animal tissues (Rothlin, 1947) and similar properties have been recorded with the mixture when tested on excised human myometrium (Rothlin and Berde, 1954). It was with this sympatholytic action in mind that Wilhelm (1951) investigated the possibilities of using Hydergine in cases of alleged cervical spasm and uterine inertia. He reported that the drug exerted a pronounced relaxant effect on the cervix in labour and that it enhanced uterine contractions by increasing their frequency and amplitude, raising tonus and regularizing rhythm. From this work, Wilhelm recommended that the first stage of labour could be considerably shortened with fractionated doses of the drug (0·075 mg. ½-hourly for 4 doses). The last point has been challenged by Law (1954) who, from a well-reasoned statistical study, was unable to demonstrate any significant difference in the length of labour in patients treated with Hydergine in the doses employed by Wilhelm, and those given an inert control substance.

Percheson and Carroll (1954) have also claimed that Hydergine hastens the course of protracted labour. They reported that the drug, in doses up to 0·3 mg. by slow intravenous injection, produced full dilatation of the cervix within 20 minutes in 70 out of 110 cases, but they failed to record the dilatation of the cervix before the drug was given. There was no foetal or maternal mortality but there were 4 cases of pronounced foetal bradycardia and an oxytocic response was noted in one instance. More recently, Jeffcoate and Wilson (1955) have reported that hourly injections of 0·15 mg. of Hydergine (up to 4 doses) had no significant effect on the length of normal labour in 59 patients compared with 50 untreated controls. In inefficient uterine action their results were inconclusive, but from clinical observations and a short series of external tocographic recordings in labour, these workers concluded that the hydrogenation of the ergot alkaloids in the preparation of Hydergine does not deprive them of their oxytocic action.

Methods

Following the methods described in an earlier paper (Embrey and Garrett, 1955), graphic records of contractility have been obtained from the puerperal uterus in 40 healthy volunteer patients. The external tocograph described by one of us (Embrey, 1955) was chiefly used in the early days of the puerperium, while the older intra-uterine balloon method of Moir (1932) was reserved for a few cases later in the lying-in period.

After a suitable control period, the drug to be studied was given and the recording continued for upwards of 45 minutes. At first only the intravenous route was used, each drug being employed in gradually increasing dosage in the light of accumulated experience. Dihydroergotoxine alone has been given by intramuscular injection, as the other preparations were not available in a sufficiently small volume to make this route practicable.

Results

Both Hydergine and its constituent alkaloids were found to be very active in stimulating the puerperal uterine contractions. It can be said without reserve that these substances possess considerable oxytocic properties, qualitatively resembling those of ergotoxine, ergotamine and dihydroergotamine but quantitatively somewhat weaker. Typical responses are seen in Figs. 1, 2 and 3.

With smaller doses, increases in frequency and amplitude alone were observed. Larger doses produced a more definite contraction pattern with marked increases in frequency and amplitude, together with an increase of tone as indicated by a rise in the base-line. This culminated in a merging of the rapid contractions producing a uterine spasm which later gave place to strong, regular but slower contractions as the spasm waned.

The time of onset of oxytocic activity naturally

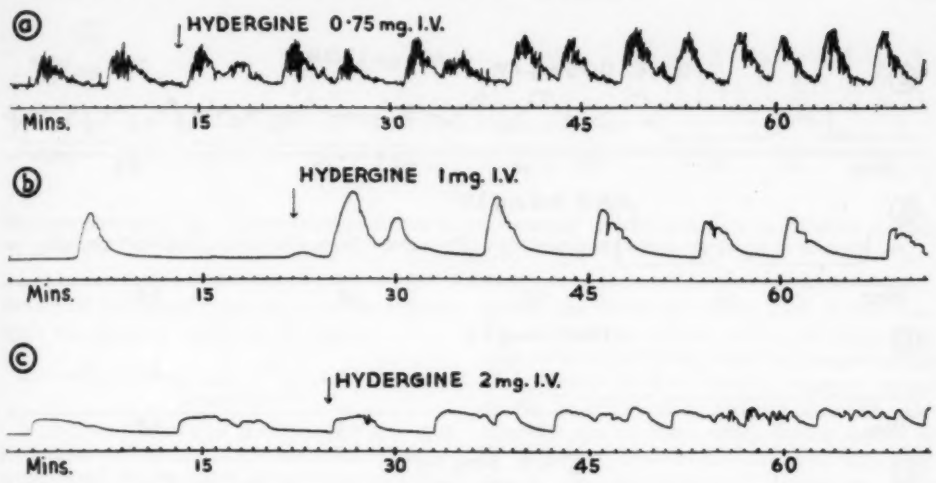

FIG. 1

The effect of varying doses of "Hydergine" on the intact puerperal uterus. Note that in (*c*) the onset of definite spasm is delayed ½-hour.

depended on the dosage of the drug. In this respect, by intravenous injection, dihydroergotoxine was not unlike dihydroergotamine and ergotoxine, while dihydroergocristine and dihydroergokryptine tended to be somewhat slower in action. The duration of activity was commonly over 45 minutes.

By allotting arbitrary units, with dihydroergotamine as standard, an approximate quantitative comparison of the oxytocic activity of the several slow-acting ergot alkaloids may be made. Table I indicating this comparison is based on over 80 records comprising those of the present series, those of an earlier investigation of dihydroergotamine (Embrey and Garrett, 1955), and tracings from the well-known researches on ergotoxine and ergotamine by Moir (1932).

TABLE I

Approximate Quantitative Comparison of the Oxytocic Activity of the Slow-acting Ergot Alkaloids

Ergotamine*	2·0
Ergotoxine*	2·0
Dihydroergotamine†	1·0
Dihydroergotoxine (*syn.* dihydroergocornine)	1·0
Dihydroergocristine	0·2
Dihydroergokryptine	0·2
"Hydergine"‡	0·4

* from Moir (1932).
† from Embrey and Garrett (1955).
‡ a mixture of equal parts of d.h.-ergotoxine, d.h.-ergocristine and d.h.-ergokryptine.

In constructing the table we have relied on a classification of the tracings by inspection alone. It was felt that planimetric analysis as used by Schild and Myerscough (1955) could not fairly be applied to external recordings, influenced as they are by so many extraneous factors. It should be noted that the table gives a comparison between the *slow*-acting alkaloids only; the *quick*-acting alkaloids, ergometrine and methylergometrine, are qualitatively dissimilar and are therefore not included.

Dihydroergotoxine and dihydroergotamine are equiactive oxytocics while dihydroergocristine and dihydroergokryptine each share but one-fifth of this power. Hydergine, the mixture of equal parts of dihydroergotoxine, dihydroergocristine and dihydroergokryptine, has two-fifths the oxytocic activity of dihydroergotamine, the standard, while the parent alkaloids, ergotoxine and ergotamine, have twice this activity.

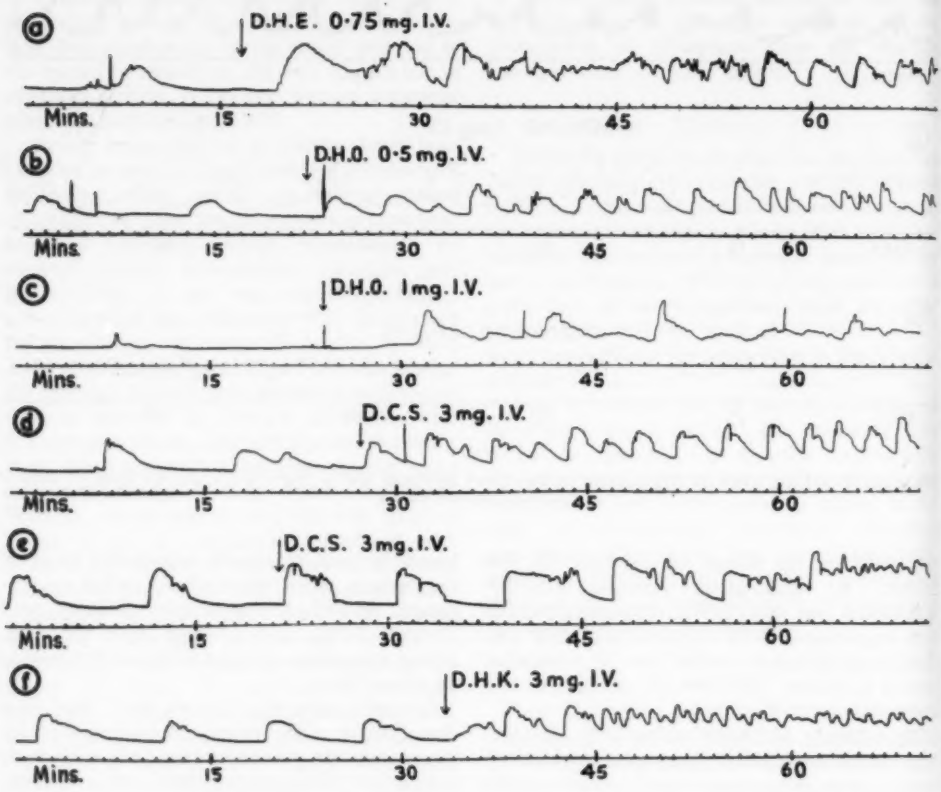

FIG. 2

The effect of:

(*a*) Dihydroergotamine 0·75 mg. I.V. A characteristic oxytocic response is induced. Note the increase in frequency and amplitude of contractions together with uterine spasm as indicated by a rise in the base-line (from Embrey and Garrett, 1955).

(*b*) Dihydroergotoxine 0·5 mg. I.V. Both frequency and amplitude are markedly increased.

(*c*) Dihydroergotoxine 1 mg. I.V. An oxytocic effect with obvious uterine spasm is induced in a virtually quiescent uterus.

(*d*) Dihydroergocristine 3 mg. I.V. The increased uterine activity closely resembles that seen in (*b*), but in this case the dose is 6 times greater.

(*e*) Dihydroergocristine 3 mg. I.V. Note that the onset of uterine spasm is delayed more than ½-hour.

(*f*) Dihydroergokryptine 3 mg. I.V. A marked oxytocic response.

(All doses refer to the drugs as their methanesulphonates.)

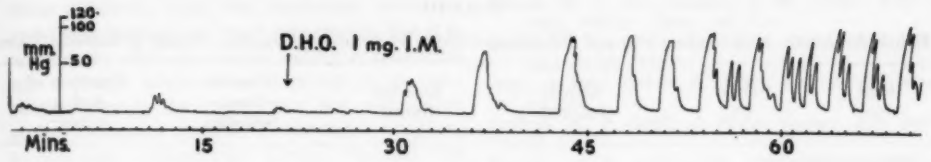

FIG. 3

Dihydroergotoxine (1 mg. of the methanesulphonate) by intramuscular injection induces a characteristic oxytocic response. This tracing closely resembles those obtained with the parent alkaloid ergotoxine by Moir (1932).

Details of individual experiments in the present work are given in Tables II, III and IV.

COMMENTS

With the evidence now presented it is seen that Hydergine and its constituent alkaloids dihydroergotoxine, dihydroergocristine and dihydroergokryptine—like dihydroergotamine—are all direct oxytocics. The imprudence of using these drugs for their sympatholytic activity in labour thus becomes apparent.

It could conceivably be argued that the use of those members of the group with comparatively little oxytocic activity yet powerful sympatholytic properties, might be within the bounds of safety. To this we would reply that the oxytocic response in a particular case is never quite predictable and occasionally an alarming response has followed a small dose of the drug. The tumultuous uterine activity resulting from such an effect in labour, with the possible sequel of stillbirth or even uterine rupture would clearly be undesirable, and we therefore consider the use of these drugs during labour to be definitely contra-indicated. For the same reason, the application of Hydergine as a hypotensive drug in the treatment of toxaemia of pregnancy, as practised by Rupp (1953) and Sauter and Suenderhauf (1954), involves an unnecessary hazard.

Compared with ergometrine and methylergometrine, which by intravenous injection are effective in less than a minute, the naturally occurring alkaloids ergotamine and ergotoxine and their semi-synthetic derivatives, are noticeably slower in action. It may be no more than conjecture to correlate the speed of action of

TABLE II

"Hydergine" by Intravenous Injection. Details of Individual Cases

Case No.	Dose I.V.	Activity Induced	Base-line Raised	Time of Onset (minutes)	Duration of Activity (minutes)
"Hydergine":					
1	0·5 mg.	0	0	Nil	Nil
2	0·5 mg.	+	0	16	16
3	0·75 mg.	+	0	20	55+
4	0·75 mg.	+	0	19	?
5	1·0 mg.	+	0	5	45+
6	1·0 mg.	+	+	10	60+
7	1·5 mg.	+	0	10	36+
8	1·5 mg.	+	0	13	24+
9	2·0 mg.	+	+	3	45+
10	2·0 mg.	+	+	8	30+
11	3·0 mg.	+	+	4	41+
12	3·0 mg.	+	+	1	45+

+=Stimulation 0=No effect

TABLE III

Dihydroergotoxine, Dihydroergocristine and Dihydroergokryptine by Intravenous Injection. Details of Individual Cases

Case No.	Dose I.V.	Activity Induced	Base-line Raised	Time of Onset (minutes)	Duration of Activity (minutes)
Dihydroergotoxine:					
13	0·25 mg.	0	0	Nil	Nil
14	0·25 mg.	+	0	9	15(?)
15	0·5 mg.	+	0	13	37+
16	0·5 mg.	+	0	3	45+
17	0·5 mg.	+	+	5	45+
18	0·5 mg.	+	+	2	31
19	1·0 mg.	0	0	Nil	Nil
20	1·0 mg.	+	+	14	55+
21	1·0 mg.	+	+	7	40+
22	1·0 mg.	+	+	7	43+
23	1·0 mg.	+	+	6	42+
24	1·0 mg.	+	+	3	45
Dihydroergocristine:					
25	1·0 mg.	+	0	19	42+
26	1·0 mg.	+	0	29	40+
27	2·0 mg.	+	0	8	13(?)
28	2·0 mg.	+	+	5	60+
29	3·0 mg.	+	+	19	40+
30	3·0 mg.	+	+	4	40+
Dihydroergokryptine:					
31	1·0 mg.	0	0	Nil	Nil
32	1·0 mg.	0	0	Nil	Nil
33	1·0 mg.	+	0	32	33+
34	2·0 mg.	+	0	20	47+
35	2·0 mg.	+	+	3	53+
36	3·0 mg.	+	+	4	35+

+ = Stimulation 0 = No effect

TABLE IV

Dihydroergotoxine by Intramuscular Injection. Details of Individual Cases

Case No.	Dose I.M.	Activity Induced	Base-line Raised	Time of Onset (minutes)	Duration of Activity (minutes)
Dihydroergotoxine:					
37	1·0 mg.	0	0	Nil*	Nil
38	1·0 mg.	+	+	15	70+
39	1·0 mg.	+	+	19	57+
40	1·0 mg.	+	0	72	30+

+ = Stimulation 0 = No effect * Nil in 50 minutes (cf. Case No. 40).

these alkaloids with their molecular structure and the complexity of their side-chains. But it is noteworthy that the rapidly acting ergometrine has a simple amino-ethanol group in its side-chain, whereas the ergotamine and ergotoxine group molecules possess, in the same position, a complete polypeptide group. Perhaps the delay in onset of action with the ergotamine and ergotoxine derivatives is to be explained by the necessity for the large polypeptide side-chain to be broken down in the body to some simpler radical before becoming effective.

Summary

(1) The hydrogenated forms of the various members of the ergotoxine group of alkaloids have been tested on the intact human uterus in 40 puerperal patients. Despite assertions that have been made to the contrary, each alkaloid has been found to exhibit active direct oxytocic properties.

(2) The possible danger of using these drugs in pregnant patients for their sympatholytic or hypotensive properties in incoordinate uterine action and toxaemia, respectively, is stressed.

(3) A possible explanation of the observed delayed onset of action with these drugs, is presented.

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VESICO-VAGINAL FISTULAE

A Report on the Vaginal Repair of 160 Cases

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VESICO-VAGINAL fistula, or modification of this type of fistula, is one of the most unfortunate accidents of pregnancy which can befall the parturient woman. On 21st June, 1949, 100 years had elapsed since J. Marian Sims, using his speculum, position and silver wire sutures was able finally to close the fistula of a slave girl after 30 unsuccessful operations.

It is well known that Sims devoted the major part of his professional career to the solving of the difficult problem of repair of urinary fistulae, and he achieved outstanding success considering the manifold difficulties with which he had to contend. Sims operated on 261 cases of fistulae and claimed success in 215, a really exceptional achievement.

The problem of repair of urinary fistula has exercised the minds and talents of many surgeons the world over since the time of Sims, and the literature is amply supplied with articles reporting results using specific suture materials, anaesthesia and antibacterials.

It is apparent from a survey of the literature on the subject that the origin of vesico-vaginal fistula is changing, as obstetric skill and facilities become more readily available to the patient in labour. Very few reports on obstetrically produced fistulae are to be found. Instead, the type of fistula which is now harassing the surgeon of today is that produced as the result of extensive gynaecological surgery and that following treatment of carcinoma of the cervix with radium.

This report deals with a series of fistulae occurring in women attending the gynaecological wards of Baragwanath Hospital during the last 3½ years.

MATERIAL

A group of 160 patients comprises the material of this report. These women had 188 fistulae which were vesico-vaginal, urethro-vaginal or vesico-cervico-vaginal in type. Every patient, who attended the hospital with this complaint, was included in the series without any selection whatever.

Patients were referred to the hospital from practically all parts of the Transvaal Province, and a few found their own way there from other Provinces and the Protectorates.

The fistulae occurred in African women, who had, in most instances, no skilled obstetric assistance at the time of confinement.

AGE AND PARITY OF PATIENTS

The age of the patients varied considerably; the youngest girl in the group was 11 years of age and the oldest was 70 years old. It is a peculiar accident of chance that these 2 patients had vesico-vaginal fistulae which were not the result of obstetric trauma.

The average age of the women in the series was 23·5 years, but the bulk of patients were in the age group 18 to 26 years.

The majority of patients were primiparous (80 per cent) and the remainder were para 1 and 2 (18 per cent). Only 2 (2 per cent) had more than 2 pregnancies.

ORIGIN OF THE FISTULAE

In 157 patients the fistulae were the direct result of difficult, prolonged or neglected labours, and 3 were caused by other means. The exceptions to the general trend were as follows. The

first occurred in a girl, 11 years of age, whose fistula was caused by a bladder stone eroding through the bladder and vaginal walls. The second case resulted after a Gaertners cyst had been inexpertly dissected out, and the third fistula was the result of breakdown of lymphopathia venereum infiltration of the vesico-vaginal septum.

In 94 instances labour had been conducted at the home of the patient and at no time was trained obstetric assistance available to her. The duration of these prolonged unassisted and obstructed labours varied considerably. One patient had been bearing down, urged on by her grandmother, for 6 days prior to admission to the hospital. She developed a fistula as a further complication to a ruptured uterus. A fair average of the duration of labour was 3 days.

There were 63 patients who had prolonged and obstructed labours in their own homes, who were then removed to some country hospital and labour terminated by forceps extractions, craniotomy, decapitation, internal version or Caesarean section. Obstetric forceps had been badly applied to 12 of these patients and were the cause of the fistula, because these patients stated that they had commenced to leak urine, via the vagina, immediately.

The Type, Number and Size of the Fistulae

Some patients had more than one fistula; the total number of individual fistulae was 188. One patient had a group of 5 fistulae scattered over an area which could be covered by a half crown piece, while several had 2 or 3 fistulae in the anterior vaginal wall. A common combination found in the patients with multiple fistulae was vesico-vaginal and urethro-vaginal types.

Type of Fistula	Number of Fistulae
Vesico-vaginal fistula	152
Urethro-vaginal	35
Vesico-cervico-vaginal	1
Total	188

The size of each fistula varied very much from patient to patient, the smallest one was the size of a pinhole and the largest measured 3 inches by 4 inches. The average size, however, was a fistula which measured 1 inch across. Characteristically the fistulae were situated in the midline of the anterior vaginal wall or just to one side of the midline, and, on an average, 1 to 1½ inches from the external urinary meatus. It was found that, when the fistula was situated less than one inch from the external urinary meatus, it was unusual for the repair to be successful at the first attempt. The further the fistula was situated from the meatus, the better the ultimate prognosis.

A feature of the fistulae comprising this series was the extensive scar-tissue formation present. The edges of the fistula and the area immediately surrounding it often had the consistency of cartilage. Thick bands of scar-tissue stretching from the breech in the vagina to the edges of the vaginal introitus, often immobilized the area and reduced the depth of the vagina very markedly. Of the patients in this group, 150 had marked to gross scarring in and around the vagina, while in 16 patients the vagina was almost completely occluded, with a small aperture at the apex of the scar-tissue mass, through which urine dribbled away constantly.

Scar-tissue was always more dense and bloodless in those patients who had been subjected to operation at other hospitals and these patients often required more than one operation before the fistula could be closed successfully.

In all cases in whom the perineum and vulval area had been bathed in urine for a protracted period, excoriation of the skin had resulted, which permitted the deposition of crystals on the pubic hair and on the sodden flakes of skin around the fourchette area.

Duration of the Fistula

The fistulae had been in existence in these patients on an average for 20·8 months. The longest duration was 96 months and shortest period was 1 month. Since there are not many centres attempting the difficult and painstaking repair, it was inevitable that many of these poor souls should become resigned to their fate.

Further Complications

A common complication accompanying the urinary fistula was recto-vaginal fistula and

third degree perineal lacerations. In 29 patients a third degree laceration was present, and 19 patients had a recto-vaginal fistula. The recto-vaginal fistulae were converted into third degree lacerations and the latter were repaired after the vesico-vaginal fistula had been closed.

There were 15 patients who developed foot-drop subsequent to the delivery of the child and in only 7 had obstetric instruments been used at the end of a prolonged labour. It is probable that the damage had already been done prior to the application of the forceps. In one case the double trauma, foot-drop and vesical fistula, had been caused by badly applied forceps, because the patient leaked urine immediately and lost control of the flexor muscles of the leg.

The Pre-operative Period

In 140 patients, the fistula had been present for a period exceeding 1 month and the condition of these patients on admission was extremely poor. The vulval region was badly excoriated, the vaginal tissue was sodden and often covered by slough and crystals, in addition in some cases foot-drop and 3rd degree lacerations were present as further complications.

Thus, before these patients could be subjected to operative procedures, an extended period of preparation was necessary. It was assumed that some degree of urinary infection was present and this was treated by means of the sulphonamide group of drugs. In a small number of cases Streptomycin was necessary to bring the infection under control. Patients with foot-drop were attended to by the physiotherapists and those with recto-vaginal fistulae or third degree lacerations were put on to low residue diets and sulphaguanadine in order to reduce soiling of the vaginal area. The vulval excoriations and patches of crystals responded to thrice daily sitz baths followed by the use of a dusting powder.

A high protein diet was ordered for the patients and vitamin supplements were used liberally.

Finally, an intravenous pyelogram was obtained in order to assess renal function and to attempt to outline the bladder. It was found in a large number of patients that bladder capacity was severely reduced.

The Operation

After the period of preparation the patient was taken to the theatre where a spinal anaesthetic was given. The patient was put into the lithotomy position and the vulva and vagina cleaned with cetavlon 5 per cent solution and draped with sterile cloths in the usual manner.

An Auvard's weighted speculum was introduced, if possible, into the vagina in order to effect maximum exposure. In the cases in whom vaginal stenosis existed, it was necessary to cut through the constricting bands of fibrous tissue and to use an episiotomy incision before adequate exposure of the fistula could be effected. The fistula was visualized and described for the records, the size, shape and position confirmed and the surrounding tissue tested for mobility. In several cases, on attempting to pass a probe or sound via the urethra and out by the fistula, stricture was found in the proximal part of the urethra; this was broken down and a catheter inserted.

If the fistula or the tissue in its immediate neighbourhood was not mobile suitably placed relaxing incisions were used to obtain the required mobility.

An area of approximately one-quarter of an inch on the periphery of the fistula was denuded of vaginal skin, care being exercised to remove only the epithelium and no deeper tissue. The lower border was denuded first in order to have a clear field at all times. The blood which flowed from the cut edges was allowed to collect in the posterior fornix and was removed by means of suction—in order to keep swabbing of the fistulous area to a minimum. At this stage a self-retaining catheter was introduced into the bladder, often under vision, and the position of the bulb checked in relation to the ultimate suture line.

The suture material used on the first 20 cases of this series was No. 1 chromic catgut. In these cases a Reverdin's needle was used to place the sutures, but was abandoned later because the needle was often far too thick for the very thin tissue to be stitched and, most important, the threading of the needle by the assistant required a high degree of skill, which often was lacking.

In the place of the Reverdin's needle and holder—a Hagedorn needle holder was used.

This permitted a smaller sized, threaded cutting needle to be used and consequently lighter weight gut Number 2 "O"—and still had the advantage of holding the needle so that the point was directed forwards and at right angles to the denuded area.

The needle was directed through the denuded area, including the whole of the vesico-vaginal septum—but not penetrating the bladder mucosa. A good sized "bite" of tissue was taken in order to have tissue in the stitch with a good blood supply—and to prevent "cutting out" of the catgut in this thin material (Diagram 1, No. I).

This needle holder was a very necessary part of the equipment because the type of person who suffered a fistula as the result of obstetric trauma was one who had a very narrow outlet, with acute subpubic angle and narrow intertuberous diameter. The lack of operating space was often further impinged upon by scar-tissue bands, vaginal stenosis and marked shortening of the vagina itself. The conventional needle holders, such as the Thompson-Walker, could not be used with any degree of accuracy.

The requisite number of sutures were placed as described above, and the end of the gut held in artery forceps until all sutures were in position. The gut was then tied, commencing with the central stitch and working outwards—using a double "true" reef knot and the excess gut cut off "on the knot" to reduce the amount of foreign material as far as possible (Diagram 1, No. II). In the earlier cases of the series, the first knot was held by an assistant using the tips of artery forceps placed across the knot, in order to reduce traction on the tissues while tying the knot. Later this step was abandoned, because it was felt that slight trauma to the lighter gut may have damaged the suture material and accounted for one or two failures at repair.

On completion of the first layer of sutures, a measured amount of sterile water was introduced into the bladder via the self-retaining catheter, in order to test the suture line. The amount of water used varied between 8 and 16 ounces with an average of 10 ounces. In 99 per cent of the cases there was no leak of water via the fistula at this stage of the operation.

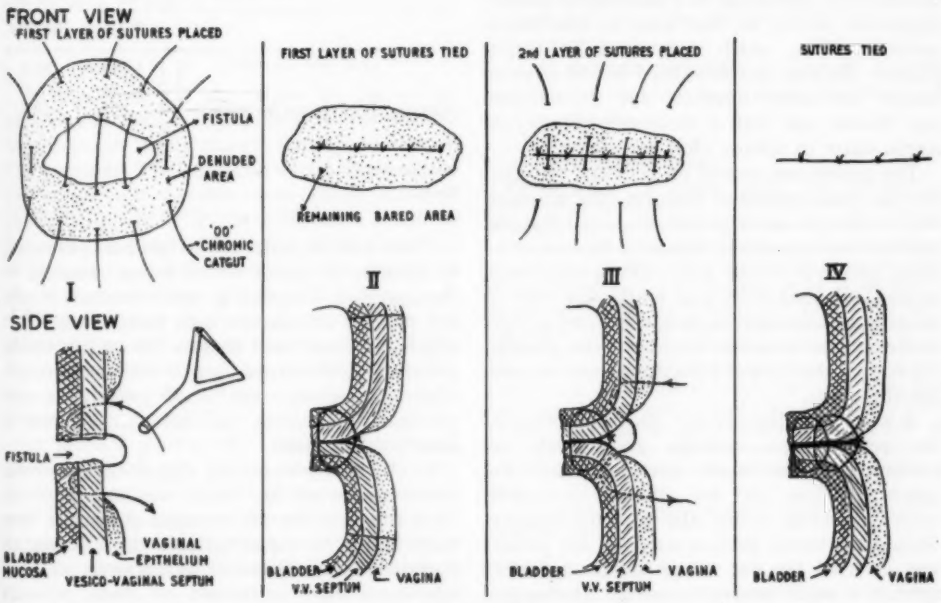

DIAGRAM 1

The second layer of sutures was now introduced. The point of the needle entered the intact vaginal squamous epithelium approximately 1/16 inch above the remaining denuded area, emerged in the denuded area about 1/16 inch above the first line of sutures and between the tied knots. The needle then repeated the manœuvre described—but in the reverse direction on the lower border of the fistula (Diagram 1, No. III). These sutures were placed in their correct position and held until all were inserted. Once again the stitches were tied from the centre outwards, using double "reef" knots and cut short (Diagram 1, No. IV).

The vagina was then cleaned of blood and clot, and carefully plugged with vaseline gauze (which was removed in 3 to 5 days). The self-retaining catheter was anchored to a mattress suture placed through the labia majora at the level of the external urinary meatus.

Post-operative Treatment

On arrival in the ward the self-retaining catheter was connected to a continuous suction apparatus similar to that used in continuous gastric suction, which maintained an empty bladder. Suction was continued for 14 days or longer, and every alternate day the catheter was flushed out with a measured quantity of sterile water to remove clots and debris.

The patient was nursed on her back throughout the whole period of bed rest, and although she was free to move in bed, we found that the catheter was not ever in jeopardy, because of its being anchored to the labia. The urinary antiseptics, sulphonamides and antibiotics used in the pre-operative period, were continued as long as the catheter remained in the bladder. Finally, a great aid during this trying time, was occupational therapy.

A week after the catheter had been removed the patient was carefully and gently re-examined. If the fistula was closed and the suture line firm, she was allowed home with advice regarding coitus and personal hygiene. Should the fistula have re-occurred the patient was deferred for one month before a further attempt at repair was contemplated. During this interim period, the vulval toilet was maintained in order to prevent the re-occurrence of the urinary type of vulvitis previously described.

Duration of Hospital Stay

The average duration of stay in hospital of the patients in this series was 57·3 days. The range was between 11 days in the simpler type of fistula to 264 days in the difficult type. However the average patient was confined to bed only for 1 or 2 periods of 14 days and the rest of the time in hospital was spent in the extensive pre-operative period of preparation or the deferred operation on those cases requiring more than one attempt at repair.

Number of Operations Required to Effect Closure

The 158 patients in this group were subjected to 212 operations before the fistulae could be closed. Table I summarizes the number of operations required.

Table I

		Patients	Per cent
Number of operations per patient	1	113	70·6
	2	34	15·0
	3	11	6·8
	4	2	1·3
	5	2	1·3
No operations		2	1·3
Failed		5	3·1

There were 34 patients who had been subjected to attempts at repair before being admitted to Baragwanath Hospital. In most instances it was not possible to ascertain how many attempts at repair had been tried because the patient could not distinguish between repair and examination under anaesthesia—but in 20 patients it was possible to establish the fact that at least 3 attempts had failed.

In all these patients the degree of scar-tissue formation round the fistula was very marked. This supports the oft repeated statement that each failure to repair reduces the chances of eventual success. However, in this series multiple operations were performed on many patients before closure could be effected, but it is admitted

that each operation became just a little more difficult.

Stress Incontinence

This complication followed repair of the fistulae in 38 cases. The prime cause for the occurrence of this condition was found to be contraction of scar-tissue in the region of the external urinary meatus. Stress incontinence was almost a certain sequela to the repair of a fistula situated near the urinary meatus. In effecting repair of this type of fistula healing often pulled the urethral meatus open and this patulous meatus allowed urine to escape on coughing, sneezing or straining. In 37 patients the incontinence responded to simple measures such as reconstruction of the external urinary meatus by freeing the tension caused by scar-tissue, or by employing the Kelly type of repair for stress incontinence. In only 1 case was it impossible to cure stress incontinence after repair of a huge fistula, and the disability caused by this complication of fistula repair was so great that the patient requested operation designed to divert the urinary stream.

Results of Vaginal Repair

In this series of 160 fistulae of the vesico-vaginal and urethro-vaginal types it was possible to operate on the fistulae via the vaginal route in 158 instances. The 2 cases on whom no operation for repair was possible were those who, on examination under anaesthesia, were found to have no vestige of urethra, plus extreme scarring of the vagina, which precluded any attempt at reconstruction of the urethra.

Vaginal repair of these 2 fistulae was not attempted and the ureters were transplanted into the sigmoid colon and the patients were discharged from hospital in a satisfactory condition (Cases 1 and 2).

In the 158 patients who had vaginal repair, closure was effected in 153 instances after one or more operations. In 3 patients (Cases 4, 6 and 7) it was considered impossible to repair the fistula after several attempts had failed. Failure to effect closure in these cases was due solely to the fact that the tissue in the region of the fistula was deficient, because the sloughing process had destroyed too large an area of vaginal and bladder walls. Consequently the suture line was subjected to a marked degree of tension during the healing process and tension is the biggest single factor in the causation of failure of repair of vesico-vaginal fistulae.

In the fourth case (Case 5) a severe and intractable stress incontinence developed after the vesico-vaginal fistula had been closed. This incontinence resisted several attempts at repair and since this complication is as incapacitating as a fistula, the ureters were implanted into a loop of ileum.

The fifth case (Case 3) was one in which one attempt at repair of the fistula was undertaken without success. This fistula could have been closed, but because a protracted stay in hospital was not possible for financial reasons, the patient requested the operation of ureteric transplant.

Thus, there were 5 failures in 158 vaginal repairs of the fistulae—a failure rate of 3·1 per cent.

If the case which, in the opinion of the operator, could have been repaired successfully, is excluded, then the corrected failure rate is 2·5 per cent.

It is thought advisable to include a brief summary of the cases in which the fistulae could not be repaired.

Case 1. (No vaginal repair)

Caroline, aged 30 years, para-8 was admitted to hospital on 18th September, 1952. There was a history of prolonged labour, unassisted, 3 years ago. She leaked urine soon after the birth of the dead foetus and had been to a country hospital where an attempt at repair failed on two occasions. On examination under anaesthesia it was found that the labia majora and minora had fused together (? failed colpoclysis by previous operator) the vagina was 1 inch in depth with gross scarring present. The opening through which urine was leaking was situated one inch above the anus. The fused labia were split open, but no urethra at all could be found. In view of the short vagina, gross scarring and absence of urethra, the vaginal approach was abandoned and her ureters were transplanted immediately into the sigmoid colon.

The patient was discharged on 24th November, 1952 quite satisfactory.

Case 2. (No vaginal repair)

Betty, aged 24 years, a primipara, was admitted to hospital on 20th March, 1953. There was a history of a

prolonged unassisted labour in 1952. She leaked urine soon after the delivery of a stillborn foetus. On examination under anaesthesia it was discovered that the vagina was grossly scarred and the fistula opening was at bladder neck. No urethra could be found. Immediate transplant of ureters into the sigmoid was carried out.

She was discharged on 4th April, 1952 satisfactory.

Case 3

Augustine, aged 22 years, a primipara, was admitted to hospital on 25th July, 1952. There was a history of a difficult prolonged labour at home in Basutoland. After 6 days she was brought to a Mission Hospital where the foetus was extracted with forceps. She leaked urine immediately. She had developed a right foot drop. On examination under anaesthesia the vulva was very severely excoriated and the vagina extensively scarred. The fistula was one inch in diameter, one inch from the external urinary meatus. She had one operation. The fistula re-opened partially. Because the patient was being charged full rates (non-resident of Transvaal) and, at request of the husband, the ureters were transplanted at first opportunity.

The patient was discharged fit and well.

Case 4

Nankeng, aged 22 years, a primipara, was admitted on 20th September, 1952. There was a history of obstructed unassisted labour and rupture of uterus. Total hysterectomy was performed. After 6 weeks when all slough had separated she was taken to the theatre and E.U.A. performed. A huge fistula was found and it was seen that the whole of the vaginal portion of the posterior bladder wall was missing. One attempt at repair was made but the prognosis was hopeless. The repair broke down and at subsequent examination it was found that there was no tissue which could be used in repair. Immediate transplant of the ureters into the sigmoid was carried out. She was discharged on 5th March, 1953 fit and well.

Case 5

Chupya, aged 26 years, a primipara was admitted to hospital on 16th June, 1952. There was a history of a prolonged obstructed unassisted labour (7 days) 11 months ago. On examination a huge fistula was found measuring 3 inches by 2 inches, situated above gross vaginal scarring at the upper third of vagina. The boundaries of the fistula were the symphysis pubis and the descending rami of the pubes.

1st operation on 18th September, 1952. Mobilization using relaxing incisions. The whole fistula broke down.

2nd operation on 19th October, 1952. Again mobilized and closed. On 3rd post-operative day a junior member of the staff removed the sutures on mistaken diagnosis of ureter closure.

3rd operation on 13th November, 1952. Using a flap of the anterior lip of the cervix the fistula was closed.

4th operation on 8th January, 1953. A small residual fistula below and to the side of the external urinary meatus was closed.

5th operation on 11th February, 1953. The same small fistula as above was closed and this time healed.

She developed a very severe stress incontinence and, because of prolonged stay in hospital, she decided to discharge herself for 3 months and to return for further attempts at repair of stress incontinence. The patient remained away until 7th February, 1954. On examination the fistula was found to be closed but there was marked stress incontinence. There was marked scarring round urinary meatus and no tissue was available for repair. The urologist transplanted the ureters into the iliac sac. The patient died on the 8th post-operative day from sepsis and peripheral vascular failure.

Case 6

Martha, aged 20 years, a primipara, was admitted to hospital on 1st September, 1953. There was a history of a 2-day unassisted obstructed labour, which was terminated by forceps in her home. She leaked urine immediately. On examination the patient had 3 fistulae situated one inch behind the urinary meatus. These measured ¼ inch, 1¼ inch and ¼ of an inch.

1st operation on 17th September, 1953. Each fistula was treated individually because to convert into one would have produced a huge fistula.

2nd operation on 3rd December, 1953. All 3 fistula had recurred. They were again repaired.

3rd operation on 3rd December, 1953. Again the 3 fistulae had recurred. It was decided that there was far too much tension on the suture line which could not be relieved; if the fistula recurred transplant of the ureters was decided upon.

4th operation on 12th January, 1954. Bilateral transplant into the ileal sac was carried out.

She was discharged on 10th April, 1954 quite fit and healthy.

Case 7

Rebecca, aged 17 years, a primipara, was admitted to hospital on 29th March, 1954. There was a history of a 4-days unassisted labour on a farm. She leaked urine for one year.

On examination there was a grossly stenosed vagina virtually replaced by scar-tissue. There was less than ¼ inch from the external urinary meatus to the anterior edge of a transverse fistula one inch in diameter.

1st operation on 29th April, 1954. Great difficulty was experienced in mobilizing the fistula. It was closed in two layers. The fistula broke down.

2nd operation on 3rd June, 1954. The fistula has increased in size, and has incorporated the previous repair. It is now 1¼ inches in diameter. Very marked scarring was again found. The fistula was repaired. The prognosis was poor. The fistula broke down again.

3rd operation on 10th August, 1954. Transplant of ureters into isolated ileal sac was carried out.

She was discharged on 9th September, 1954 satisfactory.

Among the material forming this series are some interesting cases and I should like to give brief summaries of a selected few.

A patient aged 40 years had a traumatic fistula produced by the obstetrics forceps in a country hospital. The fistula was repaired successfully, but because the patient complained of persistent pain, dysuria and frequency, a cystoscopy was performed. A large bladder stone was seen, which was removed by suprapubic cystotomy. While the bladder was opened the fistula site was inspected and found to be almost invisible.

Another patient had an enormous fistula, measuring 3 inches by 2 inches, which, for all its size, was repaired at the first operation. Unfortunately a ureter was caught in the suture line and this necessitated re-implantation into the bladder. A case similar to this was a patient who had 4 attempts at closure, each time a small hole the size of a match head persisted. At the fifth operation it was discovered that the fistula was in fact the ureter opening into the vagina. The ureter was separated from the scar-tissue and successfully re-implanted into the bladder via the abdominal route.

The 3 non-obstetric fistulae are worthy of mention. The first occurred in a patient aged 70 years of age who had leaked urine for many years. She was seen by request in the surgical ward, where she had been admitted suffering from malignant melanoma of the foot. The surgeons wanted to know if the bladder was involved by secondary growth. A biopsy showed a chronic inflammatory condition, probably lymphopathia venereum. The fistula was repaired at the first attempt much to the surprise of everybody concerned.

The second case concerned a young girl who had a Gaertner's cyst removed. The mass returned some months later when she started to leak urine. The mass was removed and the urethral fistula closed at one operation. The pathological report on the mass revealed a myoblastoma.

Finally, the youngest girl in the series was aged 11 years who had been referred from the urological ward of another hospital. She had been admitted to the hospital suffering from a vesico-vaginal fistula. The urologist had performed cystoscopy and found a bladder stone about 1½ inches in diameter, which had apparently eroded the bladder and vagina. The fistula was dilated in order to remove the stone. The stone was cracked open to discover that the nucleus was a feeding bottle teat.

Summary

This report deals with 160 vesico-vaginal and urethro-vaginal fistulae which occurred in African women.

All cases except 2 were treated by vaginal operation. The exceptions did not have vaginal repair because it was felt that repair of the fistula in the absence of an urethra would be a useless procedure.

The 160 patients in the series had 188 individual fistulae which were classified as vesico-vaginal in 152 cases, urethro-vaginal in 35 cases, and vesico-cervico-vaginal in 1 case.

The size of the fistulae varied from a pin-hole orifice to a deficiency measuring 3 inches by 4 inches with an average size of 1 inch in diameter.

Gross scarring and stenosis of the vagina was a characteristic of the patients in this series.

The fistulae had been present for periods varying between 1 month and 96 months the average being 20·8 months.

Recto-vaginal fistulae were concomitant features in 19 cases and third degree perineal lacerations were present in 29 patients.

Foot drop was present in 15 patients and had occurred as a result of the recent delivery.

The average duration of stay in hospital was 57·3 days.

The number of operations required to close the fistulae varied between 1 and 5. The large majority (70·6 per cent) were closed after one operation. Fifteen per cent required 2 operations, 6·8 per cent required 3, 1·3 per cent required 4 and 1·3 per cent required 5 operations. Thirty-four patients had been operated upon previously at other hospitals.

Stress incontinence resulted in 38 patients, following the vaginal repair. The incontinence was cured in 37 instances.

In the series 96·9 per cent of patients were discharged from hospital cured following vaginal repair of the fistula. In 3·1 per cent of cases the

urinary stream was diverted into the bowel and continence of urine re-established. A corrected failure rate was 2·5 per cent.

The patient was considered cured of her fistula, if as a result of operation she was entirely continent of urine. Stress incontinence remaining after the fistula had been closed was considered to constitute failure and only when this symptom had been removed was the patient considered a cured case.

Finally, 1 maternal death occurred in the series. This patient had intractable stress and her ureters were transplanted into an ileal sac. She died as a result of electrolyte imbalance.

Conclusions

Vesico-vaginal fistula is an extremely common complication of labour in the Bantu women of South Africa. The reasons for this are, partly the lack of adequate facilities and trained personnel available to women in labour, partly the definitely smaller pelvis of the African women. This latter factor leads to an increase in obstructed and prolonged labour which causes pressure necrosis of the bladder and vagina resulting in large fistulae, when the slough separates.

The main features which characterized the fistulae of this series were the extensive loss of tissue, the large fistulae resulting and the gross scar-tissue formation around the fistulous site and in the vagina. The Bantu people have a predilection for healing by the formation of excessive scar-tissue and the formation of keloid, and this factor adds greatly to the difficulties of repair via the vaginal route.

The repair of the fistulae in this series was, in the great majority of cases, an extremely arduous task. The average time required for operation was between 1 and 2 hours per patient, with a range from 45 minutes to 3 hours.

Nevertheless, in the 160 cases comprising this series, vaginal repair was attempted in 158 instances, and the results demonstrate the possibilities of this route as a means of relieving the condition.

There is no doubt that a certain degree of skill is required in the operation of repair, but the chief requirement is, most certainly, a patient and meticulous attitude, since the outcome of even the simplest operation is very often unfavourable. The operation should only be undertaken where adequate and proper theatre facilities and trained nursing staff are available to the surgeon and patient. The operation of repair must never be undertaken lightly, as each failure to close the fistula jeopardizes the eventual result.

Transplant of the ureters should not be resorted to until it has been proved beyond all doubt that the fistula cannot be repaired, or that intractable stress incontinence has resulted. In spite of the fact that the operation of ureter transplantation is simple, the results are often poor. The patient often suffers as a result of electrolyte imbalance, and chronic ill-health is a frequent sequela. A new type of ureter transplantation has been used in which a loop of ileum is isolated and one end brought out on the surface of the skin. The ureters are transplanted into this sac and consequently the urine which flows into the sac is discharged immediately into a colostomy bag. This type of transplant overcomes the problem of re-absorption of electrolytes, and that of ascending infection.

The flap-splitting procedure was never used in this series because it was felt that, due to the destruction of large portions of bladder wall and vaginal epithelium, it was not wise to risk the possibility of further loss of tissue in the event of failure to close the fistulae at the first operation.

For this reason, the simple method first described by Sims has been utilized. This method of repair does not endanger the remaining tissue in the event of failure, and in this series only one patient developed a fistula larger than the original one as a result of surgical intervention.

The method of simple denudation and apposition of raw areas by sutures is an adequate means of repair of vesico-vaginal fistula and is borne out by the results of this series.

The use of 2 "O" chromic catgut has proved most successful. In the earlier cases, No. 1 chromic catgut had been used and there was a greater incidence of breakdowns. An important step in the operation is the avoidance of perforation of the bladder mucosa. It was felt that a large number of residual pin-hole fistulae had resulted from the tracking of urine alongside

these sutures. The healing of the fistula occurred with a minimum of fibrous tissue and the suture line was found to be more flexible in the cases in which the lighter weight catgut had been used.

The lithotomy position together with the use of wide relaxing incisions was found to be most satisfactory, for both patient and surgeon. On a few occasions the prone position was used, but since spinal anaesthesia was routine, the patients were not comfortable and this position was abandoned.

The most important adjunct to the actual operation was the post-operative nursing. Here it is found imperative to maintain the bladder in an empty state by means of suction drainage. Passive drainage was not sufficient since the contact of urine on the suture line led to breakdown.

The supine position was essential for the same reason, and in addition the patient was far more comfortable. This active bladder suction drainage was maintained night and day for a minimum period of 14 days, and, where this action ceased for any reason, inevitably the fistula recurred.

Finally, it is felt that the repair of vesico-vaginal fistulae affords the patient such tremendous relief from the extremely trying symptom of constant wetness, that every effort must be made by those interested in this type of operation to meet and overcome the challenge of repair.

The operation is time-consuming, and often exasperating, and the results often disappointing, but the improvement in the mental and physical status of the cured patient is so dramatic, and the joy felt by these unfortunates is so great, that the surgeon is amply rewarded for every minute spent in the repair of vesico-vaginal fistulae.

Acknowledgments

I wish to thank Dr. J. D. Allen, Medical Superintendent, Baragwanath Hospital, Johannesburg, for permission to use Hospital records. My thanks are also due to Professor O. S. Heyns, Department of Obstetrics and Gynaecology, Medical School, Johannesburg for his encouragement and advice to me in the preparation of this article.

Finally to Mrs. P. M. Helps my grateful thanks are due for the trouble she has taken with the typescript.

Addendum

Since submitting the above manuscript a further 44 cases of vaginal fistulae have been completed. These extra cases bring the total to 204 and the failure rate is affected by the addition of 1 further case. The new rate is 2·9 per cent and corrected 2·4 per cent.

These patients required 56 operations on the fistulae to effect closure, and a further 4 operations were necessary to cure stress incontinence.

Thirty-two patients were cured after 1 operation, 9 required 2 operations and 2 patients required 3 operations. Stress incontinence developed in 4 patients.

The types of fistulae were:

40 vesico-vaginal.

3 urethro-vaginal.

1 cervico-vesico-vaginal.

There were 2 cases of foot drop and 4 recto-vaginal fistulae. An interesting complication which was present in 4 patients was a split urethra. Fortunately this was closed effectively in all instances.

A CASE OF PHYSOPYOMETRA

BY

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THE simultaneous discovery of gas and pus within the uterine cavity appears to be rather unusual. Pyometra, without recognized gas, was first described as a pathological entity by John Clarke of London in 1812 (De Wees, 1843). Since then, many papers on its aetiology, bacteriology, complications and treatment have appeared (Graham and Failla, 1940; Way and Simpson, 1941; Crisp and Clain, 1949; Corston, 1950; Carter *et al.*, 1951; Henriksen, 1952). Physometra, without recognized purulent uterine content, has frequently been reported in association with complicated labour and septic abortion (Falls, 1933; Bishop, 1935; Frostberg, 1941). The organisms concerned are usually *Clostridium welchii*, anaerobic streptococci, and *Bacterium coli*.

The first case of combined physopyometra, in association with fibroids and adenocarcinoma of the corpus uteri, was reported by Hector in 1929. This condition was diagnosed on opening the specimen post-operatively after total hysterectomy by Mr. Victor Bonney.

Caraven (1932) reported a case of physopyometra in association with carcinoma of the uterine isthmus, the presence of gas being detected at operation, when the uterus was found to be the size of a fist.

The following case of physopyometra was diagnosed by one of us (A.H.C.W.) at a routine clinic, and confirmed by X-ray examination, the pictures of which appear from the literature to be unique. At the same time some features of the case reminded us of the condition of pneumopyosalpinx reported by Purser and Young in 1948.

CASE REPORT

Mrs. G. H., aged 71, para 2, was first seen on the 28th May, 1953, at the Christie Hospital and Holt Radium Institute. She was complaining of vaginal discharge and bleeding, which had been present for 3 months. On vaginal examination an advanced carcinoma of the cervix (Stage 3, parametrium) was found, and the patient was admitted for treatment by radium insertion. She was discharged home on completion of the treatment on the 27th June, 1953.

On 24th July, 1953, she was seen again because she was complaining of constant and distressing abdominal pain and distension, which had been present for 3 weeks. On palpation of the abdomen a mass was found arising from the pelvis to 1 inch above the umbilicus. The mass was soft, but was felt to contract intermittently. The upper two-thirds was resonant to percussion, and the lower third was dull. A diagnosis of physopyometra was made. Later, X-ray examination confirmed the presence of gas and showed a fluid level (Figs. 1-3).

On vaginal examination there was no palpable evidence of efflorescent growth; the cervical canal could be recognized, and it was considered safe to undertake drainage, and the patient was therefore admitted.

The next day there was an escape of purulent fluid and gas per vaginam, with resultant marked diminution in size of the distended uterus. The bacteriological report on the fluid revealed *Staphylococcus albus* completely overgrown by a heavy growth of *Proteus vulgaris* resistant to penicillin, chlortetracycline, oxytetracycline, sulphamethazine, and sulphathiazole, but slightly sensitive to streptomycin and chloramphenicol.

After treatment with the last named antibiotic, dilatation of the cervix and drainage of the uterus was performed without incident on the 7th August, and the patient was discharged home comfortable on the 19th August, 1953.

The patient subsequently died on the 20th September, 1953, apparently without recurrence of the physopyometra.

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We are indebted to Dr. R. Ollerenshaw of the Department of Medical Illustration, Royal In-

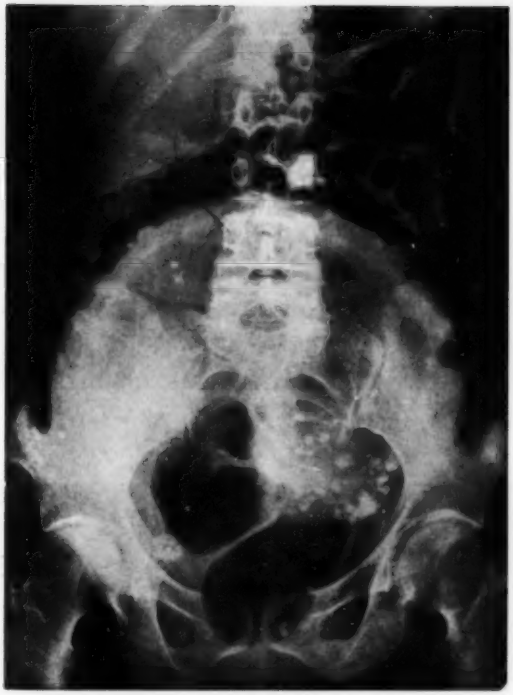

FIG. 1

A.P. supine film shows a large round soft tissue shadow arising from the pelvis, compatible with uterine enlargement.

FIG. 2
A.P. erect film confirms the presence of gas, and shows a fluid level.

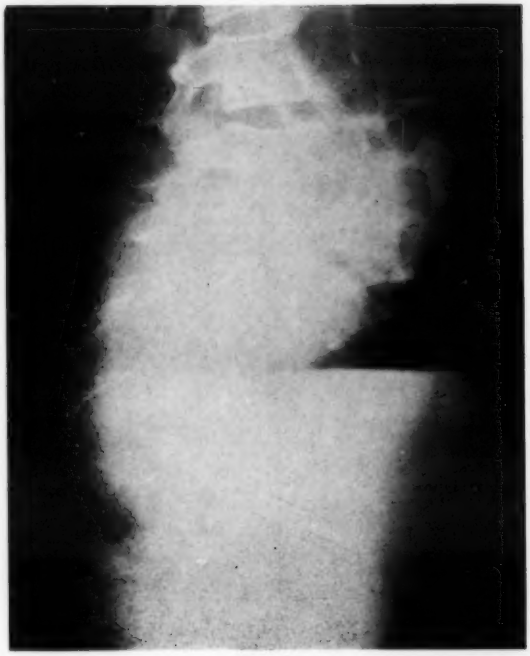

FIG. 3
Lateral erect film shows the presence of gas and a fluid level.

firmary, Manchester, for the photographs of the X-rays, and to Professor W. I. C. Morris and Dr. Ralston Paterson for permission to publish this case.

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A STUDY OF THE HISTOCHEMISTRY OF THE HUMAN FOETAL OVARY

BY

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IN a previous communication (Leckie, 1954) it has been shown that the ovary of women in the child-bearing age group contains a complex substance which is Schiff positive, sudanophilic, Gram-positive, acetone stable, chloroform stable, and non-birefringent. This material is considered to be composed of lipoid and muco-protein, the protein fraction probably containing tryptophan. It was suggested that the presence of this material is related to ovarian activity and in particular to the luteal phase of the ovarian cycle. It is, however, difficult to assess the relative importance of this substance in the adult human ovary. The normal ovary contains follicles at all phases of maturation, and, although the presence of this material may be related to certain stages in follicular development, it is equally possible that it is merely a product of degeneration. In addition, the endocrine pattern is complicated in the adult and interpretation becomes doubly difficult. The foetal ovary, on the other hand, is usually inactive and should provide some evidence regarding the possible relationship of Schiff positive material to follicular activity.

Although it is generally believed that foetal ovaries are inactive at the time of birth until puberty, cases have been reported from time to time (Novak, 1947; Govan and Mukherjee, 1950) in which varying degrees of follicular maturation have been seen. It was felt that study of similar material might prove of value in interpreting the findings in the adult ovary. At the same time opportunity has been taken to investigate the degree of activity in foetal ovaries in view of the suggestions made by Govan and Mukherjee (1950).

Material

Eighty-eight ovaries from 49 babies were obtained post-mortem, the ages varying from 24 weeks intra-uterine to 9 days postnatal: of these babies, 14 were born alive and died in the early neonatal period; 10 were stillborn at term; 21 were stillborn between 28 weeks of pregnancy and term; and 4 were stillborn under 28 weeks of pregnancy—miscarriages.

Methods

Specimens were fixed in formol-corrosive, blocked in paraffin, and sections cut at 6 μ. Thereafter the following staining techniques were employed:

(i) Haematoxylin and eosin (H. & E.)
(ii) Periodic-acid—Schiff (P.A.S.)
(iii) Acetone—P.A.S.
(iv) Sudan black.

In addition, sections were examined for birefringency.

Results

On examining the sections stained by H. & E. it was found that the ovaries could be divided into two groups—those which were apparently completely inactive, and those which showed evidence of activity as judged by multiplication in the granulosa cells, and follicular formation. By this standard 35 ovaries from 21 babies were inactive, and 53 ovaries from 28 babies showed activity. Most of these ovaries were pairs from single babies, and, invariably, it was found that the changes seen in 1 ovary of a pair were almost identical with those in its neighbour: thus the numbers may be reduced to those of the babies. In other words, activity of varying degree was

noted in the ovaries of 28 babies (57 per cent), while in the remaining 21 babies (43 per cent) no evidence of activity could be found. In both groups the foetal ages varied from miscarriages to neonatal life, and analysis suggests that activity in these ovaries is not related to age (see Table I).

TABLE I

Foetal Age at Death	Active Ovaries		Inactive Ovaries	
	No. of Cases	Per cent	No. of Cases	Per cent
Under 28 weeks	2	7·1	2	9·5
28 weeks—term	18	64·3	13	62
Neonatal ..	8	28·6	6	28·5
Total ..	28	100	21	100

On further examination, the first evidence of activity is found in the granulosa cells, which become larger, more polygonal, and more numerous. To begin with, no activity is exhibited by the ovarian stroma. When, however, the granulosa layer has reached the stage of about 4 to 8 cells in depth, there is a condensation of the surrounding stroma to form a definite thecal layer, and after formation of the atrium in the follicle these thecal cells begin to show evidence of transformation to lutein tissue. This thecal activity, however, does not quite correspond to that seen in the mature functioning ovary; instead of the cells becoming hypertrophied, epithelioid or polygonal, and having a foamy cytoplasm, generally described as theca-lutein cells, they tend to remain spindle-shaped and, although enlarged, never give the appearance suggestive of true luteinization. Where cystic atresia has occurred, the theca layer shows a closer resemblance to theca-lutein cells, but the cells are still relatively small and do not show the usual foamy cytoplasm of the fully developed luteal cells (Figs. 1 and 2).

At this stage, as there did not appear to be any relation between activity and age of the ovaries, some other factor was sought. The maternal clinical histories were studied, and it was found that, in the 28 babies with active ovaries, 21 were from mothers who had exhibited a toxaemia of pregnancy (pre-eclampsia, eclampsia, high blood pressure, accidental ante-partum haemorrhage with signs of toxaemia), 2 were miscarriages, and the remaining 5 gave maternal histories which did not seem to be relevant (external version with surgical induction, full term with intra-uterine death, foetal congenital abnormality of the bowel, maternal carcinoma of gut, foetal anencephaly with hydramnios). Of the 21 babies with apparently inactive ovaries, the maternal histories in 10 were virtually normal, 2 were miscarriages, 3 were foetal abnormalities (anencephaly), and in 6 there were histories of toxaemia (2 fulminating eclampsia, 4 mild pre-eclampsia). These findings are similar to those reported by Govan and Mukherjee (1950). To consider these findings in greater detail, attention will be given in the first instance to the active ovaries as there are no obvious changes to be found in the inactive ones.

The active ovaries in this present series fall readily into three groups, viz.: (1) toxaemic, (2) miscarriages and (3) apparently normal; the sum of these groups being 28 specimens.

1. *Toxaemic Group*

Twenty-one ovaries belonged to this group, and according to the degree of activity or follicular maturation observed, they may be considered under three headings.

Early activity. This includes every sign of activity in the developing follicle up to, but excluding antrum formation. It was the commonest finding in all of the ovaries, and was the only change found in 2 cases (9·5 per cent). The number of follicles of this early type in a single ovary varied from 1 to 45, the average being 10. In addition to these early changes 19 cases (90·5 per cent) showed more advanced activity.

Advanced activity. Under this heading are included atriated follicles. Nineteen ovaries contained follicles with well developed antra, the number of such follicles in any single ovary varying from 1 to 36, the average being 7.

Cystic atresia. Follicles which had developed and showed signs of cystic atresia were found in 13 ovaries. In each ovary they varied from 1 to 7, the average being 3.

2. *Miscarriage Group*

Two ovaries only fell into this group. In the first of these the only evidence of activity was the

presence of 1 early developing follicle. In the second, 2 follicles showed evidence of early activity, and in addition this ovary contained 1 cystic atretic follicle.

3. *Apparently Normal Group*

Five ovaries belonged to this group, and the findings in each were as follows. The first ovary contained 8 early active follicles, 2 follicles with antra, and 2 cystic atretic follicles. The second ovary contained 6 early active follicles and 1 each with an antrum and cystic atresia. The third ovary contained 1 early active follicle alone. The fourth ovary contained 3 early active follicles and 3 cystic atretic follicles. The fifth ovary contained 2 early active follicles and 1 follicle with an antrum.

The detailed findings of the above groups are analyzed in Table II. From this table it is obvious that foetal ovarian activity in all stages may be found in normal and toxaemic pregnancy, but the degree of activity tends to be greater in the presence of toxaemia. This can be seen from the columns dealing with the range and the average for each phase of the developing follicle. The position may be more clearly stated by comparing the incidence of foetal ovarian activity in toxaemic and non-toxaemic pregnancies. For this purpose it is necessary to study the whole group of 49 cases. As previously noted, 27 cases were toxaemic. In 6, or 22 per cent, no evidence of foetal ovarian activity could be found. The remaining 21 cases, or 78 per cent, showed varying degrees of follicular maturation. Twenty-two cases, 4 of them miscarriages, were non-toxaemic. The foetal ovaries in 15 of this group (68 per cent) were quite inactive, and only 32 per cent exhibited evidence of follicular ripening. The details are shown in Table III. This table emphasizes the fact that foetal ovarian activity is more common in toxaemic pregnancy and that the activity is of a more advanced degree.

Examination of the sections stained by the P.A.S. technique produced equally interesting results. Here again, there was adherence to the two groups mentioned above. In the 21 cases in which there was apparently no ovarian activity, all sections were Schiff negative (Fig. 3). In the 28 cases with ovarian activity, 26 showed Schiff positive material in association with follicles. The zona pellucida gave a strong positive reaction, and in addition globules lying between the granulosa cells, but apparently not contained within them, also reacted with the Schiff reagent. This appearance is similar to that found in

TABLE II

Total Active Ovaries 28									
Follicular Change	Toxaemic Group 21 Cases (75 per cent)			Miscarriage Group 2 Cases (7 per cent)			Apparently Normal 5 Cases (18 per cent)		
	No. of Cases	No. in Each Ovary		No. of Cases	No. in Each Ovary		No. of Cases	No. in Each Ovary	
		Range	Average		Range	Average		Range	Average
Early activity ..	21	1–45	10	2	1–2	1·5	5	1–8	4
Advanced activity	19	1–36	7	—	—	—	3	1–2	0·8
Cystic atresia ..	13	1– 7	3	1	1	0·5	3	1–3	1·2

TABLE III

	Toxaemic (27 Cases)	Non-toxaemic (22 Cases)
Inactive	6 cases (22 per cent)	15 cases (68 per cent)
Early activity only	2 cases (7·4 per cent)	2 cases (9 per cent)
Advanced activity	19 cases (70 per cent)	3 cases (14 per cent)
Cystic atresia	13 cases (48 per cent)	4 cases (18 per cent)

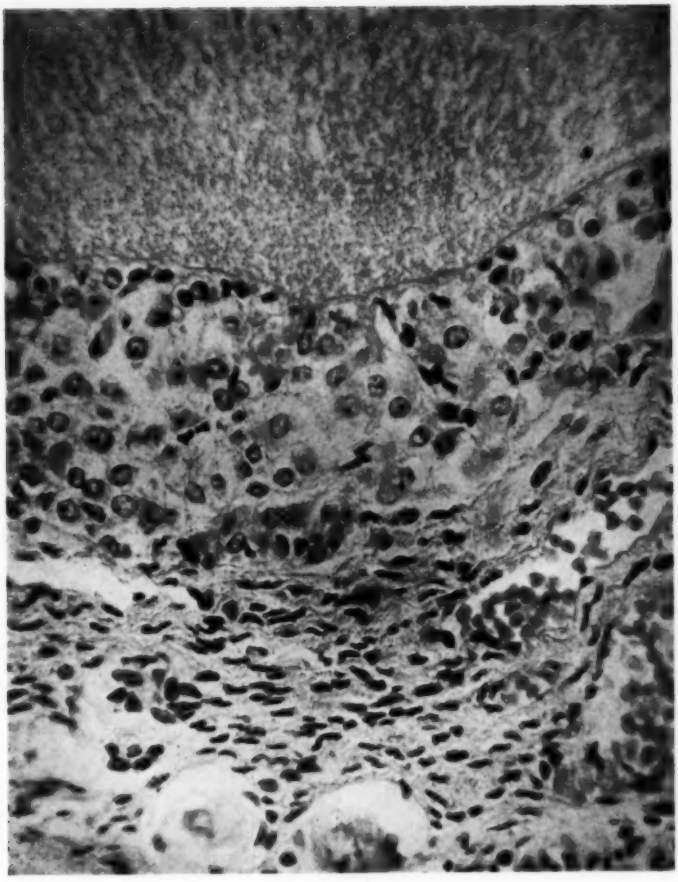

FIG. 1

Photomicrograph of active foetal ovary to show the type of theca-luteinization present: compare with Fig. 2. H. & E. ×840.

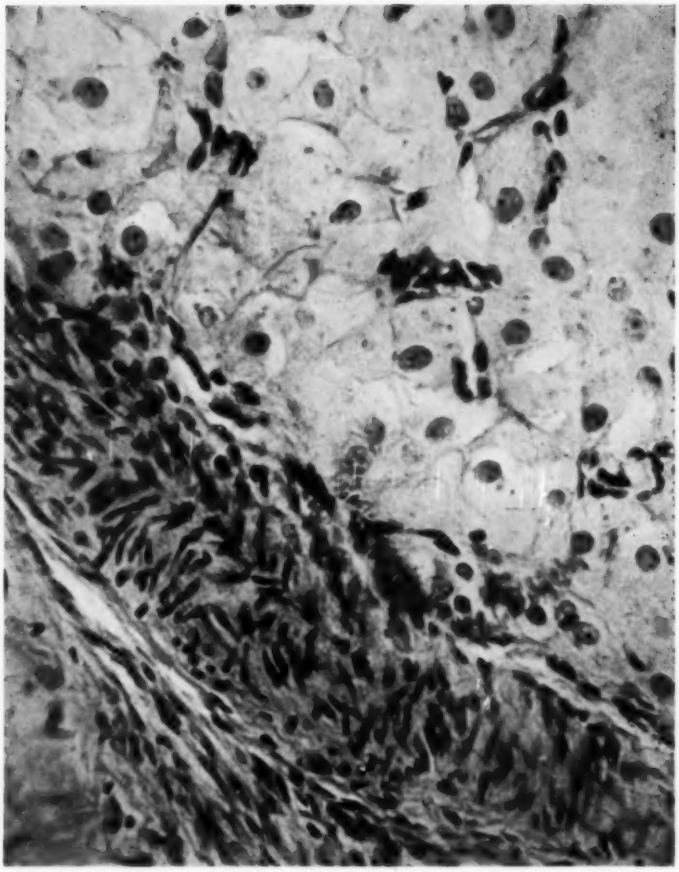

FIG. 2

Photomicrograph of active adult ovary to show theca-luteinization. Note that the magnification is the same in Figs. 1 and 2. H. & E. ×840.

F.H.L.

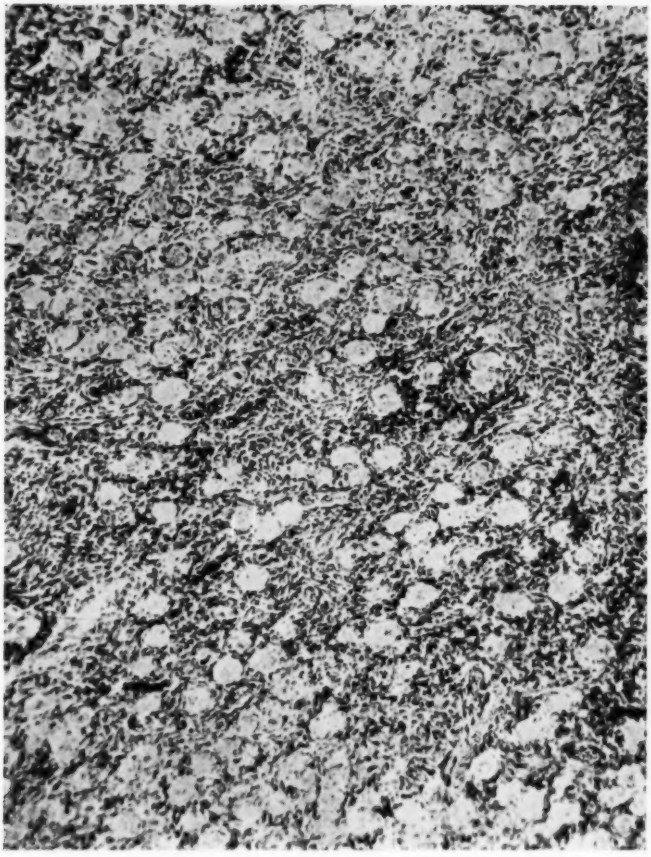

FIG. 3

Photomicrograph of ovary from the inactive group, showing numerous primordial follicles, absence of activity, and absence of any reaction to the Schiff stain. P.A.S. ×185.

FIG. 4

Photomicrograph of ovary from the active group to show an atriated follicle with globules of Schiff positive material in the granulosa layer, lying between cells, and tending to be collected near the ovum. P.A.S. ×185.

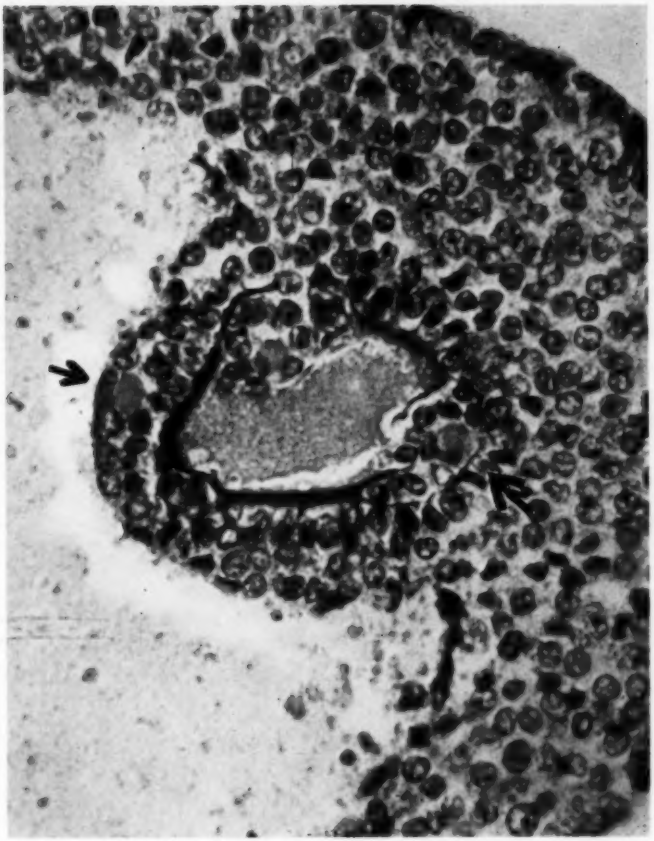

FIG. 5

High power view of cells of the discus proligerus seen in Fig. 4 to show more clearly the Schiff positive globules, 2 of which are arrowed. P.A.S. ×900.

FIG. 6

Photomicrograph of cystic atretic follicle to show Schiff positive globules in association. (Arrowed.) P.A.S. ×185.

developing follicles of mature active ovaries; in no instance was the P.A.S. positive material found in the form of granules, either intra- or extra-cellular, as found particularly in association with the corpus luteum and corpus albicans in the mature active ovary (Leckie, 1954). It was considered possible that these globules may have been derived from breakdown of the zona pellucida. However, in all the sections studied this does not seem to be the case, as the strength of the reaction and the breadth of the zona pellucida are unaltered whether Schiff positive globules are present or not in the granulosa layer.

Schiff positive globules were not found until development of the granulosa layer had reached about 6–8 cells deep; this was noted in 8 (28·6 per cent) of the 28 cases. In 19 cases developing follicles with antra were found, and Schiff positive material was detected in the granulosa layer of 18 (64·3 per cent) of these, being situated mainly in the region of the discus oöphorus (Figs. 4 and 5). In 13 cases there were cystic atretic follicles, in 3 of which there was evidence of Schiff positive material (Fig. 6). In short, out of the 28 cases with active ovaries, all but 2 revealed the presence of P.A.S. positive material in the follicular system: in 1 of the negative specimens the mother had suffered from pre-eclampsia, and in the other the condition had been hydramnios associated with anencephaly, pregnancy ending at 36 weeks.

Identification of this material was attempted by examining 11 sections of ovaries from an arbitrarily chosen 7 babies, the sections being stained by the P.A.S. technique after treating with acetone for 30 minutes. In all of these the Schiff reaction remained positive. Further sections from the same ovaries were stained by sudan black alone, and it was found that the Schiff positive material was sudan positive. Examination of these sections for birefringency was negative. These findings are similar to those observed in the mature functioning adult ovary (Leckie, 1954).

From these results it would appear that the material found only in active foetal ovaries is of the same chemical nature as that found in the adult functioning ovary. It is to be noted, however, that the Schiff positive material is in the form of extra-cellular globules, as in the follicular system of the adult ovaries, as opposed to the positive granules contained within cells which have been found in the corpora lutea and corpora albicantia of the active adult ovaries.

Discussion

Two main facts emerge from this study of the foetal ovary. In the first instance it is obvious that follicle maturation up to the stage of commencing theca luteinization is not an uncommon finding, and secondly this follicular activity is associated with the appearance of Schiff positive material in the granulosa layer.

The follicular activity may be found in either normal or abnormal pregnancy but the incidence and degree of maturation is most pronounced in the presence of toxaemia. It is generally accepted that follicle maturation occurs only under the influence of gonadotrophins and usually these are of pituitary origin (Evens, Myer and Simpson, 1932). During pregnancy, and particularly toxaemic pregnancy, there is an enormous increase in the production of gonadotrophin, and according to Smith and Smith (1939, 1940, 1941) the excess in toxaemia is of placental origin. While so-called chorionic gonadotrophin will activate the ovaries of many animals, most observers agree that it has little if any effect on the human ovary (Geist, 1933; Pratt, 1933; Hamblen, 1939; Brown, Bradbury and Metzger, 1941). It is to be noted, also, that in the present series the changes in the foetal ovaries suggest the action of a follicle stimulating hormone, and that true luteinization of the follicular cells did not occur. If Smith and Smith's interpretation is correct, it seems unlikely that the increase in gonadotrophin in toxaemia can play any part in the activity of the foetal ovaries. Accordingly, one would have to propound a primary foetal mechanism or the production of some other maternal substance which would activate the foetal pituitary. Govan and Mukherjee (1950), however, have suggested that the excess gonadotrophin found in toxaemia is in part at least of maternal pituitary origin, and that it is this substance alone which is responsible for the maturation found in the foetal ovaries. These workers have produced a certain amount of

indirect evidence of pituitary hyperactivity in toxaemia of pregnancy (Mukherjee and Govan, 1950; Mukherjee and Govan, 1951; Govan *et al.*, 1951), and more recently other workers have claimed to be able to demonstrate the origin of these gonadotrophins from the pituitary (Lajos, Szontágh and Páli, 1953a, b; Lajos, Szontágh *et al.*, 1953; Agadzhanoff, 1953). Some of these workers have also stated that the gonadotrophins in the late stages of normal pregnancy are also partly of pituitary origin and this would help to explain the occasional occurrence of foetal ovarian activity in an apparently normal pregnancy. The absence of activity in a few of the toxaemic cases is more difficult of explanation. In 2 cases the toxaemia was fulminating and resulted in the delivery of a macerated stillborn foetus. It is possible that these foetuses died before any manifestation of ovarian activity could develop. In a further 4 cases the toxaemic symptoms were very mild and the circulating gonadotrophin may have been insufficient to promote changes in the foetal ovaries. In any event a reasonably strong case can be made for the presence of gonadotrophins with a pituitary-like activity in these patients.

There seems little doubt that the Schiff positive material detected in these foetal ovaries, similar to that found in adult ovaries, is related to certain phases of follicular development. In the adult ovary, material giving a Schiff reaction was found in the granulosa layer of the developing follicle and in the cells of the fully developed corpus luteum; but in the present instance the substance was only present in the form of extracellular globules in the granulosa layer. Whether, in the globular state, it is responsible for the activity or represents merely some product resulting from this activity is as yet a matter for conjecture. It is possible that in the adult ovary we are dealing with two entirely different substances, although the similarity of their staining reactions would suggest a close chemical relationship. Arguing on this hypothesis, it is possible to suggest that the Schiff positive globules detected in the active foetal ovaries may be derived from some breakdown products, although from the findings given here it is unlikely to be from breakdown of the zona pellucida. On the other hand, the Schiff positive globules may be derived from or related to gonadotrophin, which is regarded generally as being responsible for follicular maturation. Again, it may be related to the formation of steroid substances produced in or by the follicle. In all the ovaries in which activity was noted there was no instance of true luteinization, so that it is unlikely that this material is associated with the progestational phase and formation of the corpus luteum. In fact, it has been reported already (Leckie, 1954) that in association with an active corpus luteum we find Schiff positive intra-cellular granules in addition to evidence of Schiff positive globules.

Summary

Foetal ovaries of varying age have been examined histologically and histochemically to determine if and when activity occurs in them, and to obtain corroboration, if possible, for the apparent association with activity of a histochemical Schiff positive substance which had been noted in a previous communication dealing with adult functioning ovaries.

The materials and methods have been described, and it has been shown that in this series the foetal ovaries fall into one of two almost equal groups—inactive and active. This activity or lack of activity apparently does not depend on age, but, from further studies of the case records, it has been found that the vast majority of the active foetal ovaries came from cases in which there had been maternal pregnancy toxaemia. Activity seems to start in the granulosa layer, and after maturation has progressed to or about antrum formation, activity is noted in the theca layer. It seems, however, that true luteinization does not take place in these ovaries.

Histochemical study would appear to confirm that the complex Schiff positive substance, considered to be composed of lipoid and mucoprotein, is in fact intimately associated with activity in the human ovary.

Some implications of these findings have been discussed, and it is considered that maternal pregnancy toxaemia may cause foetal ovarian activity, probably by an excess of serum gonadotrophin crossing the placental barrier to act

directly on the foetal ovary. Possible causes or source of the histochemical substance found associated with ovarian activity have been considered, but with present materials and techniques it is not yet possible to go beyond speculation.

I have to thank Dr. A. D. Telford Govan, Director of Research, Royal Maternity and Women's Hospital, Glasgow, for his unfailing advice and criticism in this study and in the preparation of this paper.

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FULL-TIME PREGNANCY AFTER PROVED ENDOMETRIAL TUBERCULOSIS

BY

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PREGNANCY, especially full-time, is rare after a woman has been proved by culture or histology to have genital tuberculosis. In fact, Stallworthy, at the British Congress of Obstetrics and Gynaecology in 1952, said that no authentic case had previously been described.

Tuberculous endometritis and pregnancy may occur together. This is shown by the 130 proved cases of congenital tuberculosis to which the *Lancet* (1952) refers. The strong assumption has been that the source of the bacillus for the foetus in many cases has been a placental lesion and in some genital tuberculous lesions have been found at post-mortem in the mother. However these lesions may have developed after conception. Thus although these conditions have been known to coexist, pregnancy, occurring after genital tuberculosis has been proved, is rare.

Continental literature contains records of several cases which were quoted by Kullander (1951). Schroeder (1921) reported 2 full-time pregnancies following proved genital tuberculosis. Cooper (quoted by Kullander, 1951) described 1 case of spontaneous rupture of a 12-weeks pregnant uterus with a tuberculous myometrium. Mensing (1936) described 1 case where a woman aged 22 years, after 4 normal confinements, aborted at the 12th week when uterine curettings showed the presence of tubercle bacilli. After treatment with intra-uterine radium, she became pregnant again within 1 year and carried to term. The cervix failed to dilate in labour, and a healthy living child was delivered by Caesarean section.

Lawrence (1939) reported 17 cases. Five of these pregnancies were full-time but 3 of the babies died with tuberculosis within a few months and 11 of the women died. He stressed the danger of pregnancy after genital tuberculosis. Kovacs (1943) found tuberculous tubes in 5 out of 390 ectopic pregnancies. Schultze (1952) described 1 case from the University sterility clinic at Greifswald. A sterile woman aged 29 years was treated with oestrogens and vitamin E after a hypoplastic uterus had been diagnosed by hysterosalpingography. Later the cervix was dilated and the uterus curetted when a tuberculous endometrium was discovered. Formalin was applied to the uterine endometrium. Two years later, the patient became pregnant and had a normal delivery of a healthy female child at term with a normal puerperium.

As few, if any, full-time pregnancies have been recorded after treatment of proved genital tuberculosis with streptomycin and para-amino salicylic acid, the following case is described.

CASE HISTORY

Mrs. C., born 12th April, 1933, was healthy until she developed a cough during her first pregnancy. There was no family or contact history of tuberculosis, but her father, a miner, had silicosis. On 15th May, 1952, Mrs. C. had a forceps delivery of a full-time child at a military hospital. This child is alive and healthy. Early in the puerperium she developed a high pyrexia with consolidation of the right lower lobe. The pyrexia persisted despite

penicillin and chloramphenicol and, on the 11th June, 1952, tubercle bacilli were cultured from her sputum. She was transferred to a sanatorium. The chest X-ray at that time showed extensive infiltration in the right lower and middle zones with enlargement of the right hilum and depression of the transverse fissure. The sedimentation rate was 86 mm. in 1 hour. The patient was considered to have a recent reactivation or progression of a primary tuberculous infection involving the right lower and middle lobes. Streptomycin 1 g. and PAS 20 g. were given daily from 1st July, 1952. Response was good and on 2nd September the streptomycin was reduced to 1 g. twice weekly until 27th October when it was discontinued, a total of 79 g. streptomycin having been given.

On 21st January, 1953, a right middle and lower lobectomy was performed by Mr. Norman Barrett at King Edward VII Sanatorium, Midhurst. At operation a number of small tubercles were seen in the remaining upper lobe. Convalescence was satisfactory and, on 14th April, 1953, Mrs. C. was transferred to West Heath Hospital, Birmingham.

Menstrual History

After a menarche at 12½ years, the periods were regular 5/28 until the first pregnancy. The first period thereafter on 31st July, 1952, was heavy with clots and associated with severe pain in the lower abdomen and groins. The next period on 18th August was less heavy and less painful. Thereafter, the periods were slightly irregular but normal and painless until the end of March, 1953 (2 months after the lobectomy). This period was very painful, requiring pethidine for relief. Two days later she had dysuria with frequency. The urine contained pus cells but ordinary culture was sterile. However, the urine cleared with sulphamezathine 15 g. given over 3 days. The next period in April was also painful. On 15th May, 1953, Mrs. C. complained of colicky pain in the left renal angle, radiating towards the hypochondrium. Sedatives, potassium citrate and hyoscyamus were given, and the pain disappeared with the onset of a heavy period 2 days later. A vaginal examination revealed an anteverted mobile uterus with normal appendages, but the cervix had a fairly severe bilateral tear. At this time, her general condition was good, the sedimentation rate being 4 mm. in 1 hour. There was no sputum and chest X-ray showed an elevated right diaphragm with an opacity suggesting a residual pleural shadow in the right costophrenic angle only.

On 26th May, 1953, under general anaesthesia, the uterus was curetted and the cervix cauterized. The curettings were examined histologically, cultures were made for *Mycobacterium tuberculosis* and guinea pigs inoculated. There was no histological evidence of tuberculosis, but the biological and cultural tests were positive. At the patient's request she was treated at home with streptomycin 1 g. and PAS 17 g. daily beginning on 2nd September, 1953. The course of drugs was rather erratic owing to vomiting, and after 50 g. streptomycin had been given the chemotherapy was discontinued on 26th October, 1953.

On 6th October, 1953, Mrs. C. complained of frequency of micturition, the urine containing some pus cells. Guinea pig inoculation was negative for tuberculosis. On 8th December, 1953, she was re-admitted to Solihull Hospital for a repeat endometrial biopsy. However, pregnancy was suspected, the last menstrual period being 14th October, 1953, the previous 4 periods having been normal and painless. Apart from slight painful bleeding on 14th January, 1954, the pregnancy progressed normally to term without alteration of the lung condition. On 20th July, 1954, Mrs. C. was admitted to Sorrento Maternity Hospital for induction of labour. The membranes were ruptured with a Drew Smythe catheter and labour commenced 3 hours later, at 3 p.m. on 24th July. When the cervix was about half dilated, the liquor became meconium stained, and the foetal heart slightly irregular. The latter improved with maternal inhalation of oxygen by mask. The cervix was fully dilated at 12.50 a.m. on 25th July, 1954. The foetal head did not advance rapidly, therefore forceps were applied after a pudendal block anaesthesia using xylocaine 1 per cent. Extraction was easy and the baby cried well after mucus had been extracted. Ergometrine 0·5 mg. was injected intravenously, and after a 12-minute third stage the placenta separated and was expelled normally. The placenta weighed 1½ pounds and contained one large infarct. It was examined for tuberculosis by both histological and cultural tests which were negative. The baby, a female, weighed 7 pounds 6 ounces.

The puerperium was normal, lactation being suppressed with stilboestrol.

On 22nd September, 1954, when seen at the postnatal clinic, Mrs. C. had had one rather heavy but painless period since delivery. Examination showed the uterus was anteverted and normal in size, the appendages felt normal and the cervix appeared healthy.

Discussion

The general course and radiological findings suggest that Mrs. C developed primary tuberculosis during her first pregnancy and that this led to a post-primary tuberculous pneumonia. This responded well to chemotherapy with streptomycin and PAS, so that a right middle and lower lobectomy could be successfully performed.

In this case the chest lesion was of considerable extent and must be considered the source of the infection of the endometrium. That haematogenous dissemination occurs at or shortly after the primary phase was shown by Choremis and Pantazis (1952) who found positive bonemarrow cultures in a high proportion of cases with a primary complex. This view is supported by Barns (1955) who discussed in full the spread of tuberculosis to the genital tract. It is possible therefore that the endometrium was affected near the onset of the

tuberculous pneumonia and that the chemotherapy given then partially controlled the disease. It is also possible that the infection occurred at the time of the lobectomy which was not covered by chemotherapy.

The exact cause of the dysmenorrhoea and heavy periods is not certain. These may be symptoms of post-partum endometrial tuberculosis as described by Sutherland (1952). Equally the cervical laceration could have accounted for these symptoms which disappeared after cervical cauterization. This view is supported by the fact that tuberculosis of the endometrium may cause no menstrual disturbance, being found only when investigating sterility due to tubal blockage.

In this case, early recognition and extended treatment with streptomycin and PAS maintained tubal patency permitting conception. Because the histological tests were negative, presumably there was only focal infection of the endometrium. The diagnosis would have been missed but for cultural and biological examination of the uterine curettings. This substantiates Vollum's observation (1954) that in order to recognize a tuberculous endometrium guinea pig inoculation must be performed because, in 10 per cent of his positive cases, histological evidence was lacking.

The threatened miscarriage may have been incidental. The foetal distress during labour may have been due to the placental infarct.

Negative tuberculous findings in the placenta and a healthy baby suggest that the genital disease has been cured.

Summary

A full-time pregnancy is described in a woman with proved tuberculosis of the endometrium, which was treated with streptomycin and PAS.

Acknowledgment

We wish to thank Dr. J. S. McKinnel who kindly undertook the pathological investigations in this case.

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PLACENTA ACCRETA ASSOCIATED WITH PLACENTA PRAEVIA

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PLACENTA accreta may occur in any part of the uterine cavity, and, although small localized areas are probably more common than is generally supposed, the diffuse form involving a large area of the placenta is comparatively rare. Herbut (1953) in a recent account of the pathology states that less than 200 proved cases have been described so far. In association with placenta praevia it is even more rare, and as far as can be discovered in the literature only 32 other cases have been recorded since 1896. The largest group, of 9 cases, was reported by Kistner, Hertig, and Reid (1952), and at the same time they reviewed the 21 previous cases. Since then 2 further cases have been reported by Stone, Donnenfeld, and Tanz (1954).

The case described here is the first case of diffuse placenta accreta to occur in the records of the North Herts Hospital covering a period of 14 years and approximately 20,000 deliveries in the area. It is recorded because of the associated placenta praevia and because we believe that the histology shows that the accretion also involved the cervix and lower uterine segment.

CASE REPORT

A 2-gravida, aged 32, was admitted to the North Herts Hospital for severe vaginal bleeding at the 26th week of pregnancy.

Previous History. She did not begin to menstruate until she was 17, but there was no evidence of endocrine abnormality and she became pregnant soon after marriage. Her first child was born on 23rd January, 1951, and after a normal delivery the placenta was expelled naturally but there was a severe post-partum haemorrhage of 50 ounces (1,420 ml.). She recovered after a blood transfusion, but 3 weeks later she was admitted for secondary post-partum haemorrhage and a curettage was performed. Some pieces of very adherent placenta were removed and no further bleeding occurred after this.

Present Pregnancy. Her last menstrual period occurred on 22nd December, 1952 and she said that she had not felt well from the beginning of pregnancy. From the 8th week she had noticed a dragging feeling in the right iliac fossa which persisted throughout the pregnancy. At the 20th week she began to have slight losses of bright blood but she did not regard this as serious until the severe bleeding which finally brought her to hospital at the 26th week.

On admission her general condition was good but there was some obvious bright vaginal bleeding with some tenderness low down on the right side of the uterus. Her blood pressure was 140/80, pulse rate 88, haemoglobin 8·5 g. per cent, blood group AB, rhesus negative. The size of the uterus corresponded with her dates and the foetus was in the vertex position with the foetal head above the pelvic brim. The foetal heart was heard. A tentative diagnosis of placenta praevia was made and she was given morphine gr. ¼.

The bleeding was gradually reduced to a brown discharge which persisted for 8 days. After this she had a further bright loss which became heavier the next day. She was given 1 pint of Group A rhesus negative blood. Further heavy painless bleeding occurred and, although the pregnancy was only of 27-weeks duration, it was decided to deliver her by Caesarean section without further examination. A second transfusion of rhesus negative blood was started before the anaesthetic and continued throughout the operation.

Operation. A general anaesthetic was administered using nitrous oxide, oxygen, and cyclopropane. After reflecting the bladder downwards a number of abnormally large vessels were seen to be running in a longitudinal direction over the surface of the lower segment which was dark in colour and surprisingly well defined for the early period of pregnancy. In order to avoid the large vessels a small longitudinal stab incision was made in the lower segment and this also entered placental tissue. The

incision was extended longitudinally by blunt stretching and the child extracted through the placenta with very little bleeding. It weighed only 2 pounds 10 ounces (1·2 Kg.) but it cried fairly well and was transferred to the premature nursery.

Ergometrine 0·5 g. was injected into the uterus. There was still very little bleeding but, as separation of the placenta did not occur in spite of firm contraction of the uterus, a manual removal was attempted. The placenta was then found to be membranaceous, extending over the whole of the lower segment, the internal os, and about ¼ of the upper segment. A portion of the placenta was separated piecemeal from the upper segment and this provoked considerable bleeding. No line of cleavage could be found and in trying to find one in the lower segment a finger was inadvertently pushed through the uterine wall which was extremely thin. Haemorrhage was now very profuse (it was estimated later that it amounted to 5 pints during the operation) and her condition rapidly deteriorated, her pulse being barely perceptible in the carotid artery. A pack was inserted into the uterus and the speed of the blood transfusion increased to a continuous flow. It was now obvious that a placenta praevia accreta had been encountered and as the pack had not controlled the bleeding a deep subtotal hysterectomy was carried out as rapidly as possible.

Progress. For 24 hours after the operation her pulse rate remained between 140 and 160 and her condition gave great anxiety. During this time, from the beginning of the operation, she received 6 pints of blood, making a total of 8 pints since the beginning of treatment. She then made steady progress, although on the 10th day of the puerperium her haemoglobin was still only 7·3 g. per cent. She was discharged a month after the operation, but the child remained in the premature nursery for a further 2 months and was finally discharged weighing 4 pounds 8 ounces (2·1 Kg.). After 18 months the child was reported to be quite normal.

Pathological Report

Description of Uterus and Placenta, after Fixation in 10 per cent formalin

A recent post-partum uterus opened anteriorly by a low vertical incision. Weight 550 g., length 17 cm., thickness of uterine wall near the fundus 3 cm. The lower portion is relatively thin, 0·5 to 1 cm., with a small ragged tear at the right lateral border. The tip of the cervix is absent. The inner surface of the lower posterior wall and of the cervical segment is ragged and several pieces of placental tissue adhere to and appear to penetrate the uterine wall.

The placenta with cord and membranes weighs 425 g. It is relatively large in diameter (28 × 25 cm.) and occupies ⅔ of the total chorion. Apart from a small area of normal thickness it is abnormally thin, less than 1 cm. in most parts, and in many areas only 2 to 3 mm. The margin is irregular. The maternal surface is torn up in many areas. The insertion of the cord is central and normal.

Histology

Sections were taken from numerous areas of the uterus. Adherent remnants of placenta were found in the whole of the posterior wall, lower segment, and cervix. Decidua vera was found only in the fundus and upper anterior wall.

In the sections from the posterior wall of the lower segment an irregular excavation of the myometrium is found suggesting erosion by chorionic tissue (Fig. 1). The decidua basalis is completely absent and remaining placental villi are found anchored direct to the myometrium, which shows a layer of fibrinoid material (Rohr's stria) facing the intervillous space (Fig. 2).

The cervix shows similar erosion of the cervical mucosa and muscularis (Fig. 3). This extends down to the lowermost edge of the placenta beyond which is normal cervical mucosa (Fig. 4). Villi are found directly attached to the muscle tissue of the cervix (Fig. 5).

In the upper part of the posterior wall poorly developed decidua basalis consisting of compact layer only is found with degenerate villi enmeshed in fibrin clot still attached. In this area there is a chronic inflammatory infiltration of the adjacent myometrium with plasma cells, lymphocytes, and a few polymorphs.

Sections from the upper anterior wall show a decidua vera of normal structure, but infiltrated with chronic inflammatory cells. This infiltration extends for some distance into the myometrium (Fig. 6). The histological structure of the placenta corresponds to 27 weeks and is normal.

Discussion

There is no really satisfactory explanation for the absence of decidua in placenta accreta, and it is surprising that it does not occur more often in association with placenta praevia because the decidual reaction in the lower segment is so often poorly developed. The relatively common post-partum bleeding in cases of placenta praevia is usually considered to be due to inefficient

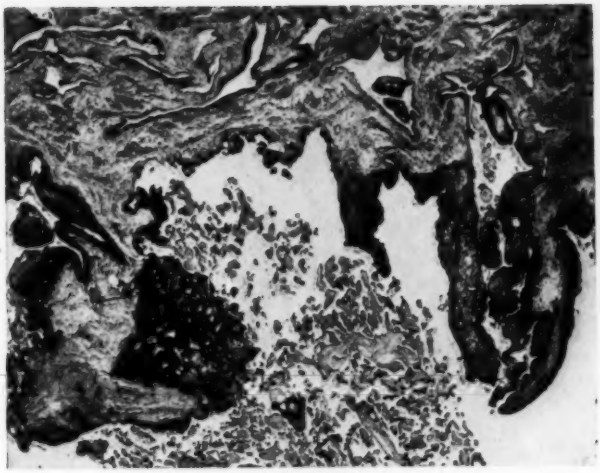

FIG. 1

Posterior wall of lower segment with adherent remnants of placenta showing erosion of the myometrium leaving myometrial projections. H. & E. ×10.

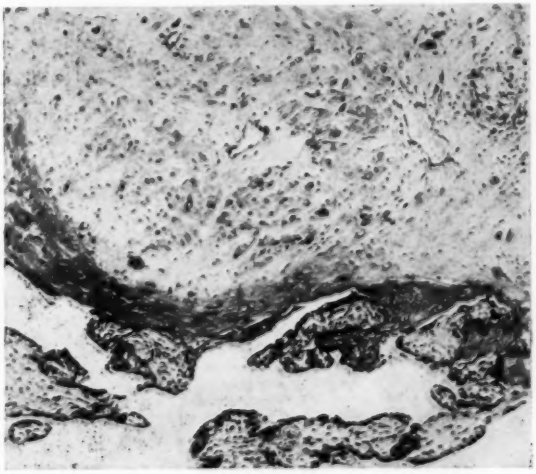

FIG. 2

Posterior wall of lower segment from the same section as Fig. 1. Showing villi anchored direct to the myometrium without intervening decidua. Only a band of fibrinoid material (Rohr's stria) is attached along the intervillous surface of the myometrium. ×128.

FIG. 3

Section from cervix showing excavation of myometrium and adherent placental tissue. Villi are seen deep in a remnant of cervical mucosa on the lower left. ×7.

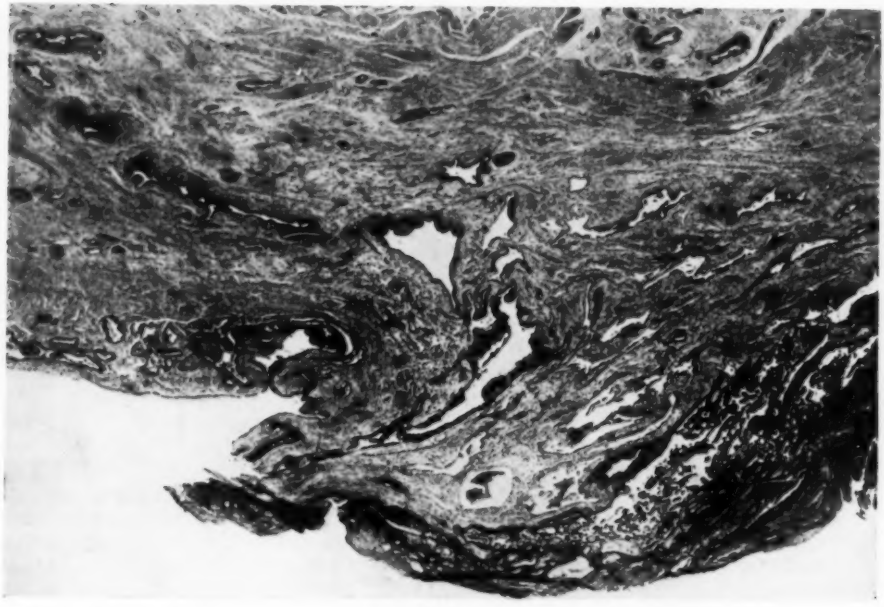

FIG. 4

Section of cervix showing lowermost margin of placenta. The cervical mucosa on the left is normal. ×8.

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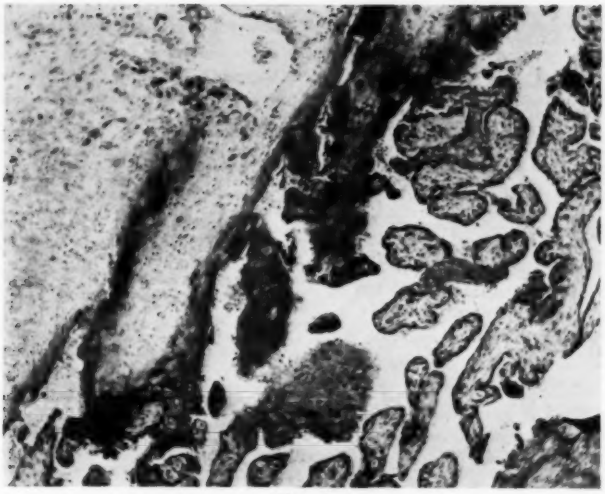

FIG. 5

Enlarged from Fig. 4. There is fusion of villi with the myometrium. ×128.

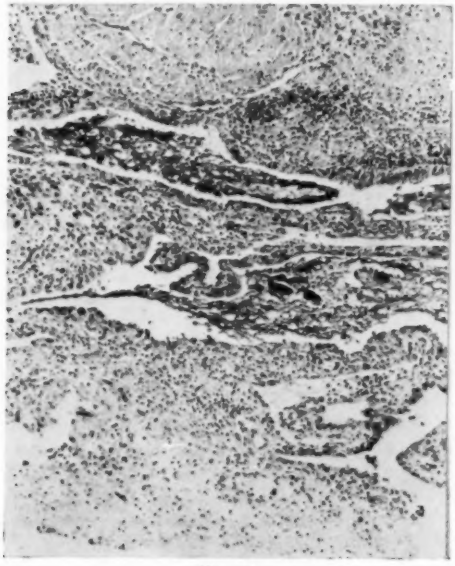

FIG. 6

Section from upper anterior wall. Decidua vera infiltrated by chronic inflammatory cells which extend into the myometrium (top portion). The mucoid material in the glands of the spongiosa shows up black. ×128.

D.W.J., K.A.M.

retraction of the lower segment. Kistner *et al.* (1952) suggest the occurrence of areas of placenta accreta in the lower segment as an alternative cause, the removal of the adherent placenta tearing open the abnormally well developed blood sinuses in the myometrium. They suggest that more extensive studies of the histology in placenta praevia would bear this out. Our case supports their view.

There is a frequent association of previous endometrial trauma with cases of placenta accreta, but it is doubtful if this is ever the primary aetiological factor. In 9 of the cases described by Kistner and his colleagues a previous Caesarean section had been performed, but large areas other than the scar were without decidua and clearly some other factor was involved. Schockaert (1940) believes that previous curettage when carried out too forcefully may cause placenta accreta. Very often, however, as in the case described here, and in fact in Schockaert's own case, the indication for previous curettage has been retained products of conception. A history of curettage may therefore only indicate that some pathological condition has existed in the decidua of a previous pregnancy.

The extent of the control exercised by the endocrine system over the development of normal decidua is not fully understood, and there is certainly no proof that placenta accreta is due to endocrine failure. The severe trauma to the placental site following attempts at manual removal in this case undoubtedly disturbed the histological picture, but the appearances described seem to indicate a chronic inflammatory origin of unknown cause.

Treatment

A brief analysis of the treatment in the 32 cases of placenta praevia accreta previously published is given in Table I.

The figures show clearly that the treatment of choice is abdominal hysterectomy, with a mortality so far of nil. It is fortunate that with the wider use of Caesarean section in cases of placenta praevia the condition will usually be discovered accidentally during the operation, thus enabling hysterectomy to be carried out at once. Conservative treatment carries with it a formidable risk and a mortality rate of at least 66 per cent. In this connexion the case reported by Gemmell (1947) and treated conservatively by marsupialization was unique in that the foetus was macerated and the uterus appeared almost avascular. One case included in the group treated by abdominal hysterectomy and reported by Chisholm (1948) was first treated conservatively, but secondary post-partum haemorrhage occurred and could not be controlled by packing so that total hysterectomy was carried out on the 19th day of the puerperium. The only case treated by immediate total hysterectomy in the above series was reported by Shotton and Taylor (1944). They describe great distension of the lower segment and they encountered severe haemorrhage during which the bladder was inadvertently injured, but complete recovery followed. Owing to the increased vascularity of the vaginal wall and the adjacent tissues a deep subtotal hysterectomy together with massive blood transfusion appears to be the safest procedure. Provided that an immediate decision is made it can be performed rapidly and without any serious difficulty.

TABLE I

Method of Treatment	No. of Cases	Alive	Dead
Manual removal and packing	11	3	8
Vaginal hysterectomy ..	3	1	2
Abdominal hysterectomy ..	17	17	0
Marsupialization of uterus	1	1	0

SUMMARY

(1) A case of placenta accreta discovered accidentally during a Caesarean section for placenta praevia is described.

(2) Treatment was by immediate subtotal hysterectomy and the transfusion of 8 pints of blood.

(3) The histology is shown by photomicrographs and it is suggested that chronic inflammatory changes were a possible aetiological factor.

(4) A brief review of 32 previously reported cases is given.

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ADVANCED EXTRA-UTERINE PREGNANCY

Fifty-two Cases

BY

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A SMALL percentage of ectopic pregnancies survive the hazards of the earlier months and advance into or towards the last trimester. The question of how this occurs is not of much clinical importance, but it is presumed that some cases are primary abdominal or ovarian pregnancies, and that in others the Fallopian tube ruptures, but the chorionic attachment is not sufficiently damaged to bring about foetal death, while in some the tube is able to expand enough to contain a full-time foetus (Frachtman, 1953).

Obviously when astonishingly large numbers of ectopic pregnancies are occurring, as in the South African urbanized Bantu, it is inevitable that the proportion of advanced abdominal pregnancies should also be relatively large.

A circular letter to 16 gynaecologists, associated with the Johannesburg non-European teaching hospitals produced details of 52 cases including those of the authors. These cases occurred mainly amongst Bantu women during the last 20 years. The condition is therefore no great rarity amongst this race.

Cases which simulate incarceration of a retroverted gravid uterus. Of the 52 cases 2 were diagnosed as incarceration of the retroverted gravid uterus. The details of one case illustrate this feature.

A young Bantu woman, 14-weeks pregnant, was admitted to hospital with vague lower abdominal pains. The uterus appeared to be retroverted and occupying the pouch of Douglas. There was marked urinary frequency but no urinary retention. This latter point should have made one hesitate to diagnose an incarcerated retroverted gravid uterus. Nevertheless, the findings on bimanual examination seemed so convincing that this diagnosis was made. Vigorous attempts were made to correct the supposed uterine malposition by putting the patient in the knee-elbow position and applying digital pressure.

This failed, and in retrospect it was surprising that a severe haemorrhage was not caused at the time. At laparotomy to "separate adhesions and correct the position of the uterus" an abdominal pregnancy situated in the pouch of Douglas was encountered. Very severe haemorrhage followed its removal, but the patient nevertheless survived. Convalescence was slow due to sepsis. This was attributable to the plugging necessary to control the operative haemorrhage.

Diagnosis during foetal viability. Only 12 cases were diagnosed while the foetus was viable. Unfortunately the diagnosis is difficult at this stage, since there may be little to suggest the unusual situation of the sac.

There may be a history of slight uterine bleeding and pain which could pass equally well for a threatened abortion or ruptured ectopic pregnancy.

Some patients complain of vague abdominal pains. Others present with symptoms suggesting subacute intestinal obstruction or peritonitis.

The textbook picture, of foetal parts that are easily felt just under the abdominal wall, was noted in only 5 cases. A sign which gave the diagnosis in the majority of cases was palpation of the uterus separate from the gestation sac, while fixity of the foetus, especially when grossly deviated from the usual subumbilical position, aroused suspicions in others. A useful test used in some cases was to inject 2 minims of pitocin intravenously. This causes a palpable hardening of a normal pregnant uterus but not of an extra-uterine sac.

The signs and symptoms of abdominal preg-

nancy have been well described by Jarcho (1949), Cross, Lester and McCain (1951), King (1954) and De Villiers (1954). In most of the cases described in the literature there is a history of pain and bleeding early in pregnancy. In over half, abdominal pain late in pregnancy is a prominent symptom. In a few cases this is described as being like labour pains.

X-ray hysterograms cannot be employed while the foetus is alive until the diagnosis is certain, and are therefore of no value at this stage.

Efforts at injecting air into the peritoneal cavity before taking X-ray photographs have not been conspicuously successful. Insertion of a uterine sound into the uterus to measure its depth may be a dangerous procedure, because the uterus is soft in an abdominal pregnancy and is easily perforated. In one case the sound passed through the uterine fundus into the gestation sac, infecting it and causing foetal death. Nevertheless this diagnostic procedure was successfully used in several cases.

The real difficulty in diagnosis before foetal death is that usually the medical attendant's suspicions are not sufficiently aroused to the possibility of an advanced ectopic pregnancy. The various wrong diagnoses mentioned in the cases reported in the literature include transverse lie, pregnancy with fibromyomata or ovarian tumours, breech presentation with contracted pelvis, ruptured uterus, postmaturity, twin pregnancy, obstructed labour, placenta praevia, double uterus, retroverted sacculated uterus, ruptured appendix in labour and ante-partum haemorrhage (De Villiers, 1954).

Unfortunately we have not yet had the opportunity of using aortograms in abdominal pregnancies. This technique should be capable of providing a conclusive diagnosis while the foetus is still alive.

Foetal Death. It is generally stated in textbooks and elsewhere that at term *spurious labour* occurs, during which the patient feels pain, and bleeds from the uterus. The foetal movements are said to become very active at this time, after which they die down and foetal death occurs.

Seventeen of our cases gave a history which suggested the possibility of spurious labour. In 3 a finding of dilatation of the cervical os was found which seemed to confirm that spurious labour had indeed occurred.

In other cases the symptoms and operative findings suggested that the "spurious labour" was due to rupture of the liquor amnii into the general peritoneal cavity, i.e., there was sudden severe pain with shoulder-tip pain and operative findings of recently ruptured membranes with the foetus lying free in the abdominal cavity.

Diagnosis after Foetal Death. Unfortunately the first untoward observation is often cessation of foetal movements, which brings the patient to the doctor. Suspicion may be aroused at once because of the history and physical signs described previously or else, at a later date, when the uterus fails to expel the foetus.

In the majority of the cases in this series the diagnosis was only made after foetal death. A pregnancy, which continues for longer than 2 months after foetal death at term, may be presumed to be an abdominal pregnancy.

X-ray examination at this stage may be helpful in showing foetal death. Absence of the uterine shadow may suggest the diagnosis, while a salpingogram showing the uterine cavity separate from the foetus is diagnostic.

Infection of the Sac Pre-operatively. In 7 cases the sac was clearly infected pre-operatively. In one the patient died of general peritonitis after laparotomy, in another the foetal bones were discharged through a sinus in the posterior vaginal fornix, which was surgically enlarged to facilitate the passage of the foetal parts. (The literature contains many isolated cases of foetal parts being discharged per rectum, per vaginam, or through the abdominal wall.)

In one case the sac was infected by injudicious efforts to measure the length of the uterine cavity with a sound.

The management of cases where the sac is infected pre-operatively will be considered under treatment.

Mummification and Calcification of the Foetus. Eight cases were diagnosed only after the foetus had undergone adipocerous changes or calcification (lithopaedions). In these cases menstruation recommences normally. On routine examination, often for sterility, a mass, separate from the uterus, may be found. A diagnosis of

fibromyomata is then usually made. The following case illustrates a diagnostic point:

A patient was admitted to Baragwanath Hospital complaining of sterility. On examination a round mass, approximately 15 cm. in diameter and presumed to be a fibroid, was found in the pouch of Douglas. This case was then examined by a medical student, who on being questioned as to his diagnosis said the mass could not be a fibroid, because it had "spikes" on it, and that it must be a lithopaedion. His point was proved by X-ray and laparotomy.

The "spikes" were easily palpable on bimanual examination, and were caused by bones protruding from the general mass.

One lithopaedion was unexpectedly found at autopsy (not included in series), another was found 20 years after the patient's 6th pregnancy had gone to term but had not ended in delivery. The patient, aged 60, was admitted to hospital for a broken leg and the abdominal mass was noticed.

Treatment of Advanced Abdominal Pregnancy. Laparotomy should be undertaken as soon as the diagnosis is made, though in rare cases with a live baby near viability it might be justifiable to postpone the operation in the hope of obtaining a live baby (Barrett, 1952). In such a case X-ray examination should first be made in an attempt to exclude foetal abnormalities which are common in abdominal pregnancies.

There is much debate in the literature regarding the *management of the placenta.* The post-operative results are certainly best when the placenta can be safely removed at operation. King (1954) in his recent series of 11 personal cases removed the placenta in all of them without fatality. Such a fortunate experience must embolden operators to attempt removal of the placenta in every case until disaster occurs.

Our series clearly shows how dangerous placental removal may be. The placenta was removed or attempts were made to remove it in 24 cases. In 8 of these this was obviously a mistaken policy, for severe haemorrhage and shock followed. There were 5 deaths from this cause.

We do not accept the statement of Kerr and Moir (1949) that, when the placenta has been dead for some time, it may be removed safely. Attempts at manual removal of a long dead placenta in 4 cases were followed by severe bleeding and shock causing death in 2.

When any doubts exist as to the safety of removing the placenta, it is wiser to leave it undisturbed, no matter whether it is dead or alive. Of the 18 cases where our records show the placenta was left undisturbed there were no deaths, and there was no case of haemorrhage.

Our series of cases also shows that another vital decision is whether to close the abdomen completely, or to pack the cavity, marsupialize it or drain it.

Apart from those patients who died from post-operative haemorrhage the worst results were obtained when the cavity was left open, by marsupializing, packing or draining. This was carried out in 13 cases. Of these only 8 need be considered because, of the remainder, 3 died shortly post-operatively and in another drainage merely amounted to dilating a sinus in the posterior vaginal fornix.

Of these 8 cases 7 developed sepsis leading to lengthy and stormy convalescence with secondary haemorrhages and the discharge of sloughs. The only patient that was drained and did not go septic was drained vaginally through the pouch of Douglas.

Obviously when there is uncontrollable haemorrhage, as in the cases that died, plugging must be employed, but it is questionable whether drainage is indicated on the grounds of pre-operative sepsis.

In one case there was marked pre-operative infection of the foetal sac and placenta, yet removal of the foetus and cord, with abdominal closure without drainage, gave an excellent result. The patient's temperature settled and she was discharged from hospital on the 10th day. She was re-admitted 6 weeks later running a slight pyrexia and with the sac distended with sero-pus. The sac was reopened and the placenta came away easily. The patient was finally discharged 2 weeks later.

Not all patients with the placenta retained were so fortunate even when there was no pre-operative sepsis and no drainage. In two cases the placenta was extruded through the abdominal wound, and in both cases convalescence was long and stormy.

Of the 18 cases where the placenta was left *in situ* (and who survived) post-operative sepsis developed in 13.

The placenta was completely and successfully removed in 21 cases. None of these went septic except 2 cases which were plugged.

In summing up, therefore, our series of cases clearly shows that the placenta should be removed when it is obviously safe to do so, e.g., when it is attached to a viscus such as ovary, tube, omentum or uterus which is easily removed *in toto*.

The abdomen should be closed without drainage even in the presence of pre-operative infection. (The sac can always be re-opened if need be.)

Prognosis for the Foetus. In our series of cases only 12 viable foetuses were born alive. Of these only 4 survived the first few days. None of these 4 was deformed.

Of 77 cases reported in the literature (De Villiers, 1954) there were 47 live-born children of whom 30 survived. Probably the urge to report cases is much stronger when the foetus is born alive!

The incidence of foetal deformities is said to be very high (18 out of the 47 live-born cases reported in the literature). Actually only 7 deformed foetuses were observed in our series. When deformities do occur they are probably due to the pressure of surrounding parts.

Three cases had deformed limbs. One case also had spina bifida and 1 had branchial cysts. In two cases there was flattening of the head.

Two cases show that a live child may be delivered after rupture of the sac with expulsion of the foetus into the general peritoneal cavity. This condition has been called "grossesse extramembraneuse" (Allen, 1954). In one case the foetus had probably been lying free in the general peritoneal cavity for several weeks. Its head was flattened on one side. Perhaps the risk of pressure deformities is increased when the foetus lies free in the abdominal cavity in this way.

Prognosis for the Mother. With judicious treatment, especially as regards the management of the placenta, and the provision of plentiful blood for transfusion, there should be very little operative mortality. There were 7 deaths in this series of 52 but some of these patients were treated before blood transfusions were freely available. Six of these deaths may be attributed to placental separation (whether intended or accidental) causing bleeding. There is, however, a considerable chance of morbidity from post-operative sepsis when the placenta is left *in situ* (13 out of 18 cases). Subacute intestinal obstruction occurred in 6 cases pre-operatively and in 1 case post-operatively.

The chances of subsequent pregnancies occurring are probably poor, though in 2 cases, in both of which the placenta had been left *in situ* and had become grossly septic, subsequent intra-uterine pregnancy occurred, followed by normal deliveries.

Fate of the Retained Placenta. When the placenta is retained and does not become infected it takes a variable time to absorb. King (1954) described a case in which he claims that the placenta took 3½ years to absorb.

In only 2 of our cases was the rate of placental absorption noted. It took 4 months for the mass to disappear in one and 2 months in the other.

Summary and Conclusions

An analysis of 52 advanced abdominal pregnancies occurring in the Johannesburg group of teaching hospitals is presented.

From this experience it is clear that the diagnosis is seldom made before foetal death, probably partly because the patient is seldom seen before foetal death.

The possibility of late abdominal pregnancy should be considered when there is a history of bleeding and pain early in pregnancy, or, later in pregnancy, vague pains suggesting intestinal obstruction. When an abdominal pregnancy is situated in the pouch of Douglas, it may closely simulate an incarcerated retroverted gravid uterus.

A sign which is diagnostic when present is palpation of the uterus separate from the pregnancy sac, while fixity of the foetus in an unusual position should arouse suspicions. After foetal death X-ray hysterosalpingograms are relatively simple, and are diagnostic. These cannot be employed before foetal death, and in such cases X-ray studies have as yet not been very successful. It is suggested that an aortogram would be valuable at this stage.

A lithopaedion may be diagnosed on bi-

manual examination by its hard "spiky" feeling. X-ray pictures clinch the diagnosis.

The material on which this paper is based suggests that spurious labour does occur in some cases with uterine contraction, bleeding and dilatation of the os. In other cases this term is incorrectly applied to the peritonismus which occurs when the liquor ruptures into the general peritoneal cavity. (The foetus may survive such an occurrence.)

The treatment of choice for most cases of advanced abdominal pregnancy, whether the foetus is dead or alive, is removal of the foetus leaving the placenta undisturbed in order to avoid dangerous bleeding. The abdomen is closed without drainage. In a minority of cases, where the whole sac can obviously be removed with safety, the placenta may be removed, thereby obviating the danger of post-operative sepsis. The fact that the placenta has been dead for some time is no indication that it may be removed safely. Drainage or marsupialization of the amniotic cavity should be avoided even in the presence of some pre-operative sepsis. Plugging should only be used if haemorrhage makes it imperative.

The prognosis for the foetus is generally poor. Only 4 live children were obtained which survived more than a few days.

The incidence of pressure deformities is appreciable.

In this series of 52 cases there were 7 maternal deaths. In 6 of these death was attributable to removal of the placenta (partial or complete) causing bleeding and shock.

The best results were obtained when the placenta was safely removed without haemorrhage and the abdomen was not drained, i.e., 16 cases with no mortality or morbidity (except for 1 patient who developed post-operative intestinal obstruction). Of the 18 cases where the placenta was left undisturbed there was post-operative pyrexia in 13. This was particularly severe in 7 of the 8 cases where the cavity was marsupialized, plugged or drained, and who survived the immediate post-operative period.

Two cases, both of whom had marked post-operative sepsis, were noted as having subsequent normal deliveries.

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AN UNUSUAL CASE OF SECONDARY ABDOMINAL PREGNANCY

BY

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THE following case of secondary abdominal pregnancy, apparently subsequent to a spontaneous rupture of the uterus, is considered to be of sufficient interest to warrant publication.

The patient, Mrs. McA., aged 31 years, a parous woman of short stature, height 4 feet 9½ inches, has a rhachitic flat pelvis. Her previous obstetric history consisted of the forceps delivery of a stillborn child in 1945 and 3 living mature children delivered by Caesarean section in 1947, 1948 and 1950. The first two operations had been by the lower segment route; at the third, dense adhesions had made the classical approach necessary. The heaviest child weighed 7 pounds 9 ounces; all the puerperia were normal.

History of the Present Pregnancy. The last menstrual period was on 19th November, 1952, the expected date of delivery being 26th August, 1953. The patient was first seen on 6th March, 1953 and in all attended the Clinic six times. On 26th June the pregnancy was noted to be "big" for the estimated duration; an X-ray was reported as follows: "Single foetus, oblique lie; the general size of the foetus indicates roughly seven-and-a-half calendar months duration." On 19th July, Mrs. McA. was admitted to hospital as an emergency on account of ante-partum haemorrhage which had commenced about one hour previously, and which had been preceded by abdominal pain during the night. The patient's general condition was fairly good. Although she appeared to be in considerable pain, chiefly in the lower abdomen, there was little or no vaginal bleeding. The blood pressure was 114/82, the pulse rate, 80, the temperature 97·4° F. On abdominal examination a swelling consistent with a 36-weeks pregnancy was noted. There was no rigidity but there was a fair amount of tenderness, mainly in the iliac fossae. No foetal heart sounds could be heard. The differential diagnosis lay between an early rupture of the uterus and a combined accidental haemorrhage.

Operation. Owing to the thin abdominal wall the peritoneal cavity was entered almost immediately. The foetal membranes, covered by omentum, were encountered next, and filled the entire incision. In the belief that the condition was due to a uterine rupture, an unsuccessful attempt was made to deliver the uterus through the wound. The amniotic sac was therefore incised with escape of a moderate amount of liquor amnii, and a stillborn female child, weighing 6 pounds 6 ounces was extracted. The child, which had been lying transversely *in utero*, had not been dead for very long. No deformities were noted, although an autopsy was not obtained. A further search showed that the placenta was not in the uterine cavity but was adherent to the outside of the fundus, extending on the right side to the posterior abdominal wall and mesentery and on the left side to the under-surface of the ribs. There had been slight bleeding from the lower extremity of the placental site at its attachment to the uterus, but otherwise bleeding was minimal. The cord was ligated with catgut close to the placenta and cut off short, the placenta being left *in situ*. The abdominal wound was closed in layers. An intravenous drip was set up in theatre and was continued after the patient's return to the ward, 40 ounces (1,136 ml.) each of glucose saline and blood being given.

Puerperium. The patient's recovery was less rapid than after a normal Caesarean section. She had some coffee-ground vomit in the first 48 hours which settled spontaneously. She complained of abdominal pain to the left of the umbilicus on the eighth day, which cleared up after another 7 days. The patient was discharged on the 21st day after operation. A Hogben test on 24th July was negative; an X-ray on 30th July showed a soft tissue swelling in the left iliac fossa.

Follow Up. On 19th August, 1953, Dr. A. Klopper of the Clinical Endocrinology Research Unit, Edinburgh, carried out two tests for pregnanediol—both were negative. On 9th January, 1954, a mass could still be felt in the left iliac fossa, but a soft tissue X-ray was negative. On 5th May hysterosalpingography was carried out and reported as follows: "The films show a uterine cavity with origin of Fallopian tubes at points marked 'X' on postero-anterior films. On the left side of the body of the uterus a projection is shown, presumably the site of previous rupture and there is a little related extravasation. Peritoneal spill from the tubes is shown in later films" (Fig. 1).

DISCUSSION

It is presumed that the abdominal pregnancy developed secondarily to a rupture of the uterus for the following reasons:

(*a*) No history suggestive of a tubal pregnancy in earlier weeks could be obtained.

FIG. 1
Postero-anterior hysterosalpingogram.

W.D.G. [560]

(*b*) At operation the lower attachment of the placenta appeared to be situated centrally over the outer surface of the uterine fundus, and not in the region of either broad ligament. It was impossible to demonstrate either Fallopian tube owing to the risk of causing haemorrhage.

(*c*) Hysterosalpingogram shows the outlines of two apparently intact Fallopian tubes, plus an additional sinus leading from the cavity of the uterus.

It is considered possible that the pregnancy may have escaped from the uterine cavity in one of two ways. Either satisfactory union of the uterine muscle did not take place after the third Caesarean section, leaving a gap through which the growing ovum protruded, or else a silent rupture took place in the early months of pregnancy. In support of the latter is the discrepancy between the expected date of delivery and the date of operation; the patient was delivered of a mature child weighing 6 pounds 6 ounces at the thirty-third week of pregnancy, as estimated from the date of her last menstrual period. The weight of this baby compares not unfavourably with that of her other full-time children, especially when the abnormal placentation is considered. If this explanation were assumed to be correct, the bleeding on 19th November, 1952 might be taken as accompanying this uterine disturbance. Unfortunately, the patient can give no accurate account of her menstrual periods prior to this date.

Summary

The case history of a patient who had a secondary abdominal pregnancy is given. An argument is presented to the effect that this pregnancy was secondary to a primary implantation in the uterine cavity, with secondary uterine rupture through an old Caesarean section scar.

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ORAL AND VULVAL ULCERATION WITH INFLAMMATION IN THE EYE

BY

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THE association of ulcers of the mouth and vulva has been recognized as a clinical entity for many years, having been first described by Neumann in 1895. More recently these two lesions have been described along with others elsewhere, notably inflammatory lesions in the eye (Whitewell, 1934; Behçet, 1937). Despite these reports, the relationship of these lesions is still not understood. Moreover, records of cases have presented so many varied features that it is certain that different conditions have been described which have nothing more in common than the sites affected. In this paper an account will first be given of the diseases which may present in this way and a case of vulval and recurrent oral ulceration will then be described and discussed.

APHTHOSIS (BEHÇET'S SYNDROME)

Aphthous ulcers of the mouth alone are common but only rarely are they found in association with similar lesions of the vulva. The ulcers themselves are small round or oval lesions, with a sloughing base and a reddened border, and they are commonly both painful and tender. They may be single or multiple and may appear simultaneously at both sites, or at either alone. Healing is usually rapid.

Occasionally either lesion may be larger and deeper, and healing is considerably delayed (White and Brain, 1947). Under these circumstances the first lesion may be a nodule deeply situated beneath the mucous membrane and skin; following central necrosis in the nodule ulceration results. In such a lesion, which may be slow to heal, the degree of induration may be more marked, whilst secondary infection in the ulcer may give rise to enlargement of the regional lymph glands. This condition has been described as Periadenitis Mucosa Necrotica Recurrens (Sutton, 1935); it is, however, probably a more severe degree of the aphthous ulceration mentioned above. Both forms of ulceration are frequently recurrent.

In addition to lesions in these two sites others may appear elsewhere, the most striking and most serious being inflammation in the eye. This combination of physical signs has been referred to as the "triple symptom complex" or "Behçet's syndrome" (Behçet, 1937). The vulval and oral lesions are identical with those just described, whilst the ocular changes may be conjunctivitis and corneal ulceration or even more extensive ones such as iritis with hypopyon or panophthalmitis. As an accompaniment to the more severe forms of the syndrome, several other manifestations are occasionally seen, such as raised painful nodules on the skin—similar to erythema nodosum—joint effusions and thrombophlebitis. It is not uncommon for the name Behçet's syndrome to be applied to ulcers of the mouth and vulva together, without ocular signs, the difference between this and the aphthosis of these regions described above being then merely one of nomenclature, it being extremely probable that they are different degrees of the same condition.

The prognosis of the condition is, however, much more serious if ocular changes are present, for, although complete recovery may occur from the initial attack, recurrences are often followed by progressive ocular destruction and perhaps blindness (France *et al.*, 1951). Occasional involvement of the central nervous system—possibly vascular in origin—has led to death (Berlin, 1944). Repeated attacks of the oral and vulval ulcers themselves can be a continued

source of pain and discomfort and perhaps deterioration in general health.

For the treatment of the more serious forms of the disease and the prevention of recurrence, Phillips and Scott (1955) advocate the use of cortisone or corticotrophin, whilst for the relief of pain and to assist healing of lesions in the mouth, Sneddon (1954) has found local application of Aureomycin solution to be valuable.

Erythema Multiforme

This is a condition principally characterized by a maculopapular rash, which is less often vesicular or bullous in type, on the extensor surfaces of the limbs, the palms and soles, and occasionally on the trunk and face. If bullous lesions appear in the mouth and on the vulva they may be easily abraded, and ulceration results. The eruption subsides and the superficial ulcers heal in 2 to 3 weeks.

A much more severe form of this disease may sometimes be seen, which mainly affects the mucosae. Widespread sloughing of the oral mucosa occurs whilst the patient might also develop purulent conjunctivitis, urethritis, balanitis in the male and vaginitis in the female. The skin rash is generally present also, but may on occasions be transient or absent. This condition is sometimes known as the Stevens–Johnson syndrome (Stevens and Johnson, 1922). Recurrence of either form is not uncommon.

The widespread sloughing of the oral mucosa seen here can be distinguished from the true painful aphthous ulcers previously described. If there are superficial vulval lesions present the typical skin rash should enable the correct diagnosis to be made. In the absence of the rash, however, differentiation might be more difficult.

The chief danger of this condition is extension of the disease into the chest from which the resulting pneumonia has been fatal (Finland, Jolliffe and Parker, 1948). Permanent damage to the eyes may occur either from scarring of the cornea and conjunctiva, or following the introduction of infection within the eye after perforation of the globe.

Aureomycin has been reported to have a dramatic effect in the severe form of erythema multiforme (Robinson, 1951; Church, 1950). Sneddon (1954) found it useful in 2 cases, but without effect in a third. Again the local lesions within the mouth have benefited from the application of Aureomycin solution.

Ocular Pemphigus

In this condition, which affects the eyes, the mouth, and the vulva, the first signs may be seen in any situation. The most characteristic changes are in the eye, which is the reason for the name the disease has received. A catarrhal inflammation is first seen in the conjunctiva, to be followed later by much scar tissue formation (Church and Sneddon, 1953). Adhesions become marked, until in the later stages the lids and globe become fixed together with resulting restriction of movement, corneal ulceration and perforation. In the mouth, intact vesicles may be seen, which, when abraded, form painless superficial erosions. Healing again occurs with considerable fibrosis. On the vulva, similar superficial erosions or vesicles occur which are also singularly painless and heal with such scarring that stenosis of the vagina may occur. Although the disease is progressive, periods of quiescence may occur, to be followed by exacerbations.

The disease affects an older age group than the preceding ones, the ages of onset in Church and Sneddon's cases being 59 to 79. This fact, combined with the relatively painless lesions in the mouth and vulva, and the widespread scarring of the healing process, helps to distinguish the condition.

The severity of the disease appears to diminish in time, but the prognosis depends on the effects of scarring which are most serious in the eyes. Although the use of Aureomycin solution has helped healing of the oral lesions, no form of treatment has been found to halt the progress of the disease.

Superficially, there is indeed a resemblance between these conditions, but closer observation of the physical signs does demonstrate significant differences between them. Although the aetiology of the three diseases is not known, our subsequent understanding of them may be increased if attempts at more precise diagnosis be made; it might then be possible to assess more

accurately the value of different forms of treatment about which there is at present some confusion.

Case Record

A nulliparous woman of 31 years attended the Gynaecological Out-Patient Department of the Jessop Hospital for Women, Sheffield, on the 27th July, 1954. She was complaining of a painful ulcer on the vulva which had been present for 7 weeks and had steadily increased in size despite various forms of local treatment and a course of penicillin injections. From time to time over a number of years she had suffered from recurrent ulcers in her mouth, but had otherwise enjoyed good health. She had never been out of Great Britain, and although her husband had been abroad during the war, he had not been away for over 5 years.

On examination, she was found to have a large, oval, shallow ulcer measuring 2 by 1 inches, replacing two-thirds of the left labium majus and minus (Fig. 1). The ulcer had a punched out appearance, a reddened margin, and a yellow sloughing base. On palpation there was little induration but considerable tenderness. One or two small glands could be felt in the left groin but none was palpable in the right. She was admitted to hospital the following day for further investigation.

On general examination no abnormality was discovered beyond the labial ulcer and a raised temperature to 99° F. From the investigations performed, the following results were obtained. Dark ground illumination failed to show spirochaetes and the Wassermann Reaction and Kahn Test were negative; smears from the ulcer surface showed only the presence of *Staphylococcus pyogenes* and *Bacterium coli*, insensitive to penicillin, streptomycin, and aureomycin; no acid-fast bacilli could be demonstrated; an X-ray of the chest showed no evidence of tuberculosis. A biopsy was taken from two places on the ulcer edge, the report upon which read:

> "Microscopically the appearance is that of a simple ulcer. There is a considerable amount of acute inflammatory granulation tissue lining the ulcer. In the connective tissue of the ulcer wall there is also considerable infiltration by lymphocytes indicating chronic inflammation. The lymphocytes show diffuse infiltration as well as perivascular and perifollicular arrangement. Macrophages are fairly numerous and eosinophil polymorphs are in moderate number. Plasma cells, however, are not in evidence. The appearance is not suggestive of either tuberculous or syphilitic infection, though neither can be excluded. No evidence of malignancy is detected."

Various methods of treatment were employed. Aureomycin cream was applied locally to the ulcer surface in the initial stages, after the above tests had been carried out and whilst results were awaited. During this period, the local pain and discomfort became greatly diminished and at one point on the margin healing began slowly to take place. Progress seemed so slow, however, that local treatment with aureomycin was stopped, and 3 times daily bathing with 1/6000 potassium permanganate was substituted whilst at the same time a 6-day course of sulphamezathine was given by mouth. No improvement occurred, and the ulcer began to be more painful again. The effect was tried of Stabilarsan 0·45 g. intravenously, but the ulcer became more painful still, and a generalized rash appeared on the body. The rash subsided after the arsenic was stopped, and 3 injections of B.A.L. 1 g. were given.

By this time the ulcer was larger and more painful than on admission, measuring in fact 2·1×1·2 inches. Moreover, as the diagnosis was still uncertain and treatment had been ineffective, a small meeting was called of consultants concerned (gynaecology, pathology, dermatology, and venereology being represented) to discuss the case, and formulate a plan of action. At this meeting the diagnosis of Behçet's syndrome was agreed, and treatment by local application of aureomycin was decided upon. On 4th September, 1954, treatment was begun with 3 times daily painting with aureomycin 250 mg. in 10 ml. water, and over this an application of aureomycin cream was placed. On the 13th September the ulcer was reduced in size to 1·5×0·8 inches, and by the 20th September it was completely healed. Whilst under this regime, however, the patient developed an ulcer on the left side of her tongue, which healed after 8 to 9 days. She was discharged on 25th September, 1954.

She has been seen on several occasions since, and, although there have been no further vulval lesions, she has continued to have ulcers within her mouth (Fig. 2). Sometimes, one, sometimes several have been present, and on one occasion she had one measuring 1 cm. in diameter. Although this aspect of her illness causes her discomfort, her present fear is a return of the genital lesion. So frightened is she that this might recur that no intercourse has taken place since discharge from hospital over 4 months previously.

Discussion

The appearances of the ulcers of both mouth and vulva in this case indicate clearly that the diagnosis is that of aphthous ulceration (Behçet's syndrome). The extent and indolence of the vulval lesion did not resemble the superficial transient erosions of erythema multiforme, and the discrete painful mouth lesions were quite unlike the widespread sloughing of the oral mucosa which is seen in the more severe form of that condition. Similarly, the painful nature of the ulcers, the absence of significant scarring following healing, the absence of ocular changes, and the age of onset made ocular pemphigus most unlikely.

In considering the vulval lesion alone, syphilis, tuberculosis and malignant disease were thought the least improbable, although in appearance the ulcer did not greatly resemble

FIG. 2
Aphthous oral ulcer. Behçet's syndrome.

FIG. 1
Aphthous vulval ulcer. Behçet's syndrome.

any, whilst the similarity to lymphogranuloma inguinale or granuloma venereum seemed smaller still. Laboratory examination, moreover, quickly excluded the more common conditions.

With the diagnosis made of Behçet's syndrome without as yet ocular changes, the important question in prognosis arises as to the likelihood of such changes subsequently appearing. Although there are by now a considerable number of cases on record in which all three signs appeared, there are many in which oral and genital lesions were the only ones present. No doubt also the more serious cases with ocular involvement have been reported more frequently than the milder cases. It cannot be denied, however, that in this case the later development of eye signs is a distinct possibility. Moreover, as the patient is still having ulcers in the mouth, the process whatever it may be is still active and a recurrence of vulval ulceration must be regarded as not unlikely.

From the standpoint of treatment, making the correct diagnosis may well be important even though we do not as yet understand the cause of the condition, and have no specific treatment to offer. The available evidence suggests, however, that we are dealing with a generalized disease process and that general treatment is most likely to be effective. Any radical local measures are therefore not indicated, however tempting this line of approach may appear. In the present case, for instance, the possibility of excision of the ulcer followed by skin grafting was considered before the diagnosis was made. It is very doubtful if operative treatment of this sort would materially assist the immediate condition, and it would almost certainly confer no lasting benefit. In the case described by Curth (1946) a plastic operation on the vulva did nothing to prevent recurrence in later years.

There has recently been an encouraging report on the value of cortisone and corticotrophin in this condition (Phillips and Scott, 1955). Using cortisone acetate by mouth in doses of 50 to 75 mg. daily, or corticotrophin 25 to 60 mg. daily by injection, episodes of ulceration and ocular inflammation settled down well. It may be that therapy of this nature might have assisted healing in this case. The benefit which was obtained from the local application of Aureomycin solution is in accordance with the experience of Sneddon (1954) who used the drug in cases of oral aphthous ulceration with good results. The success of the drug in the present case is somewhat difficult to understand in view of the fact that only organisms resistant to it were obtained from the ulcer surface; it may be, however, that the drug acts here in quite a different way from its antibiotic effect.

Two important unanswered questions seem to remain after consideration of this case. The first is how is the case to be investigated further, and the second is what treatment is indicated at present in order to minimize the risk of recurrence? No satisfactory answer to the first can be given; virus and bacteriological studies already carried out have so far not materially increased our understanding of the disease. The answer to the second might lie in the recent experience of Phillips and Scott (1955) who have provided some evidence that recurrence may be prevented by the continued use of cortisone or corticotrophin. Should any further serious relapse occur in this case, the effect of this form of therapy should no doubt be tried. The necessity of attempting to minimize the risk of recurrence of a manifestation as incapacitating as the vulval ulcer is borne out by the fact that, although the patient had been able to tolerate well the continued discomfort of repeated oral ulcers, the thought that another vulval ulcer might appear caused her great distress; the pain she had experienced from it made it a disabling condition, the effect of which was not completely abolished even after it had healed.

Summary and Conclusions

Attention has been drawn to three conditions which present the triad of physical signs, ulceration of the mouth and vulva, and inflammation in the eye. These three conditions are:

(i) Behçet's syndrome: aphthous ulceration of the vulva and mouth with iritis and hypopyon.
(ii) Erythema multiforme.
(iii) Ocular pemphigus.

The characteristics of each condition have been described. In general, the aphthous oral and vulval lesions are round or oval ulcers with a

sloughing base and a reddened margin, they are painful and tender and can be distinguished from the extensive sloughs of the mouth and the superficial vulval erosions and the skin rash of erythema multiforme on the one hand, and on the other from the relatively painless oral and vulval ulcers of ocular pemphigus which heal with much scar tissue formation. The ocular changes of each condition may be more difficult to differentiate as conjunctivitis and corneal ulceration can be common to all; after healing has taken place, however, ocular pemphigus may then be evident as extensive scarring results, which limits the mobility of the eye.

A case is described in which there was a vulval ulcer which lasted for 14 weeks, in association with repeated aphthous ulceration in the mouth; the diagnosis was made of Behçet's syndrome without ocular involvement. The likelihood of subsequent ocular changes or of recurrence of the vulval lesion is discussed; the possibility of the first cannot be denied, and the second can be regarded as a not improbable. Treatment with penicillin, sulphamezathine, stabilarsan, and local bathing with potassium permanganate was unsuccessful, but the local application of Aureomycin solution and cream to the vulval ulcer led to rapid healing, although it did not prevent the reappearance of oral lesions.

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ENDOMETRIAL SARCOMA COMPLICATING CYSTIC HYPERPLASIA

With Remarks on "Carcino-sarcoma"

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THE following case seems to us both unusual and suggestive.

Mrs. R.B., a housewife and secretary, aged 42, was admitted to University College Hospital on 31st December, 1951, for investigation of irregular bleeding *per vaginam*. Her periods had begun at the age of 16 and had been normal and regular (4/28) until 2½ years previously. They then became irregular and at times shorter in duration (3–5/17–28) for 2 years. During the next 6 months they had become much heavier than ever before and there was an associated intermittent intermenstrual loss. For the last 7 weeks before admission there had been a continuous loss of blood. There had been no pregnancy although she had been hoping for a child.

On examination she was found to be an obese cheerful woman in good health, with evidence of mitral stenosis but no cardiac enlargement or diminution of exercise tolerance: her blood pressure was 170/95 millimetres of mercury. The abdomen was normal. Vaginal examination revealed a superficial central erosion of the cervix with a patulous external os through which could be seen a small polypoidal growth. The uterus was anteverted, freely mobile and enlarged to the size of an 8-weeks pregnancy.

On 1st January, 1952, an examination under anaesthesia confirmed these findings and dilatation of the cervical canal was performed. A uterine sound passed 3 inches and as the dilators were being inserted some bulky white necrotic-looking tissue came away from high up the canal. A tentative diagnosis of endocervical carcinoma was made and radium inserted accordingly (40 mg. in the intra-uterine tube and 100 mg. into the vaginal vault) for 2 days. As, however, the microscopical finding proved to be endometrial sarcoma, it was decided to remove the uterus and appendages. On 9th January, 1952, the uterus was packed with a gauze roll soaked in formalin and the cervical lips sutured together, after which an abdominal hysterectomy, together with a wide removal of both appendages and a large cuff of vagina, was performed. No evidence of any direct spread of the growth or of any nodal or hepatic involvement was discovered. Her recovery was uneventful, and careful follow-up over the subsequent 3 years has shown that she has remained extremely well, without any vaginal bleeding or discharge. Examination now reveals a short smooth vagina and rectal examination shows no abnormality. Therefore for just under 3 years she has kept well without any sign of local or general recurrence, having been last seen on 23rd December, 1954.

The *curettings* were found on section to consist of about 8 polypi of peculiar structure. They were of lobulated outline (Fig. 1), with a core of proliferating mesenchyme rather like endometrial stroma (Fig. 2), partly dense and partly loose, often with abrupt changes of density (Fig. 1). In some there were no true glands but merely surface crypts (Fig. 1); in others, glands were present but seemed distorted, stretched and narrowed by the proliferating intervening stroma (Fig. 2). Stromal mitoses were very numerous (Fig. 2), and some of them were abnormal (Fig. 3); a few were seen in the epithelium. Reticulum impregnation showed a dense, mostly pericellular network of fibres with meshes of elongated radiate pattern (Fig. 4), as if stretched by centrifugal growth, All the polypi showed a more or less marked central accumulation of congested thin-walled blood vessels (Fig. 1). A diagnosis of endometrial sarcoma was made.

One polyp was much less cellular than the others and composed of strands of hyalinizing collagen between columns of connective tissue cells. There was also a strip of more normal endometrial tissue, showing a mild metropathia, in continuity with a piece of sarcoma. The transition between the two was abrupt, with a striking change in the number of mitoses.

The *hysterectomy specimen* consisted of a complete uterus with a cuff of vagina and both adnexae. The right tube was unremarkable: the left had a pea-sized peritoneal cyst just above the ovary. The left ovary contained an average sized mature pale yellow corpus luteum. Both ovaries showed a few defunct but recent, shrunken, orange-yellow corpora lutea. The uterus was slightly enlarged, with a few seedling intramural fibroids, and the corporeal endometrium thickened by multiple tongue-like polypi suggesting classical metropathia (Fig. 5). Below these, occupying the dilated cervical canal and springing from its posterior wall, was a firm walnut-sized polyp resembling a fibroid.

Microscopically, a small area at about the centre of the uterus showed a normal secretory endometrium (Fig. 6), but the bulk of the polypoid portion had the typical gland pattern of a florid cystic hyperplasia (Fig. 7). This was of quite ordinary type, with no atypical epithelial proliferation. The stroma varied. In the upper part of the body about half of it was of the usual sort, with some local patches where the nuclei were rather large and hyperchromatic, and about half was divided up into narrow columns of cells by wavy bands of hyaline collagen. These bands stained normochromatically with toluidine blue; they are seen in Figure 7 (especially lower right). Both gland and stromal mitoses were scanty. Lower down the gland pattern remained the same, but the intervening stroma showed more mitoses, with more hyperchromatism and more nuclear variation. In addition there were patches of radium necrosis. Where the sarcomatous part began and ended was impossible to determine as there was no abrupt change in the character of the stroma. In the lower corpus the inter-glandular stroma was similar to, and continuous with, that forming the core of polypi of similar form to Figure 1, and in general was similar to Figure 8. Figure 8 is taken from the edge of the large polyp in the cervical canal. It shows a fibrosarcomatous structure, with much collagen, some quasi-epithelioid orientation, much nuclear variation and many mitoses—some of them abnormal. There were many less cellular areas and some broad patches of hyaline collagen. One sarcomatous polyp contained a few bundles of smooth muscle: no striated muscle was seen with suitable stains, nor any muscle fibres of a form suggesting striated muscle, nor any other heterotopic differentiation. There was no invasion of vessels or of the underlying uterine wall. The cervix below the large polyp was free of tumour: its glands showed some early squamous metaplasia and there was a small erosion. Both ovaries were normal on section, that from the left showing a typical mature corpus luteum as well as a shrunken specimen a few months old, walled by vacuolated cells.

Discussion

Correlation of the clinical and pathological features of this case is not easy. The patient had clearly been ovulating, and one can only attribute the development of cystic hyperplasia to some unknown cell change which at once made much of the uterus unresponsive to progesterone and issued in the aberrant formation of hyaline collagen and of sarcoma. Possibly this change resulted from a long period of anovular cycles, corresponding with the irregular menstruation which started 2½ years before admission. The final bout of 6-months menorrhagia leading to 7-weeks continuous loss could be ascribed to the progressive development of a polypoid hyperplasia and sarcoma in the new largely unresponsive mucosa.

The fact of recovery does not militate against a diagnosis of endometrial sarcoma which is a less malignant condition than the mixed mesodermal tumour. Useful figures on this point, as well as on the relative incidence and prognoses of the different uterine sarcomas, are given by Kimbrough (1934), McDonald, Broders and Counseller (1940), and Finn (1950). The histological diagnosis in the curettings was based on the grossly abnormal architecture and the stromal mitotic activity. The stromal nuclei here were within the normal (admittedly wide)

FIG. 1

Low-power view of one of the polypi obtained by curettage. It has a lobulated outline, with the glands reduced to surface indentations, a core of proliferating mesenchyme of varying density, with a central accumulation of thin-walled blood vessels. H. and E. ×18.

FIG. 2

Higher power view of polyp core, showing dense proliferating mesenchyme much like endometrial stroma. The nuclei are fairly uniform, featureless but roughly vesicular and ovoid, with scanty cytoplasm. Most of the black dots are cell divisions. The glands give the impression of being pushed aside by the proliferating stroma. H. and E. ×225.

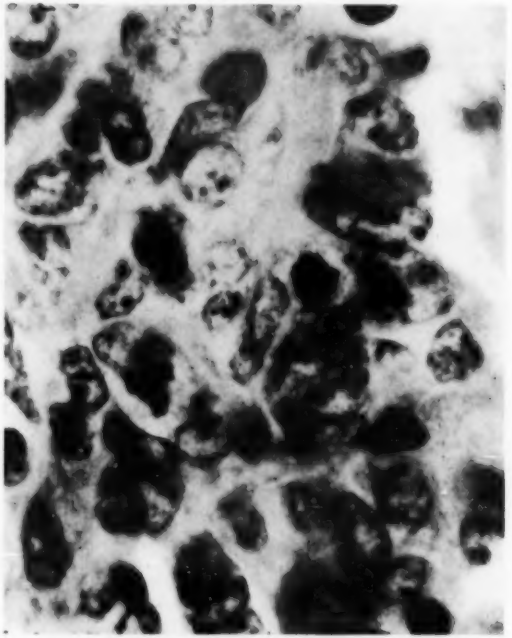

FIG. 3

Still higher power view of the proliferating stroma showing nuclear detail, with two mitoses, one of them tripolar. H. and E. ×1000.

FIG. 4

Reticulum impregnation of edge of polyp, showing roughly pericellular fibre network with meshes elongated at right angles to the epithelial surface above. Modified Gomori. ×200.

FIG. 5

The gross hysterectomy specimen. The cavity of the uterus is filled with mucosal polypi. Near the internal os a group of 4 of these can be seen nestling up against the larger darker polyp which occupies the dilated cervical canal.

FIG. 6

Section from middle of uterus, showing early secretory endometrium, with early "ferning" of gland contours, pale cytoplasm and basal nuclei. H. and E. ×100.

P.E.H., D.P.C.

FIG. 7

Section of fundus, showing gland pattern of cystic hyperplasia, with partial replacement of stroma by hyaline collagenous bands, especially at right lower corner. H. and E. ×55.

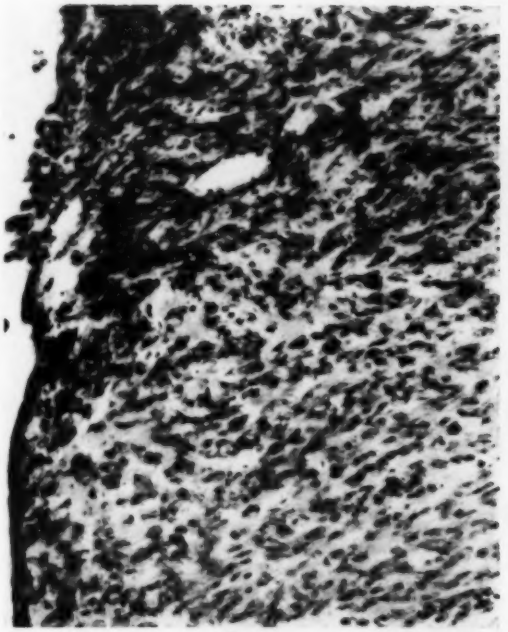

FIG. 8

Section of polyp in cervical canal, showing epithelial surface to left, variation of nuclear crowding, form, and staining depth in stroma with many cell divisions, the whole appearance suggesting a rather polymorphic fibrosarcoma. H. and E. ×150.

limits of size and staining reaction, so that the latter cell-changes were probably partly the response of the growth to irradiation; but this was probably not the whole cause, for there were some areas of uniform moderate nuclear hyperchromatism near the fundus, well away from any radium necrosis, and without any of the bizarre appearances which radiation usually induces. The hyaline areas were not thought to be osteoid. Similar changes were noted by Lomax and Anderson (1941) in a case resembling ours. We have not seen their like before in uncomplicated metropathia.

There have been 6 cases published which seem similar to ours (Felländer, 1907; Stein, 1912; Froeschmann, 1919; Strong, 1919; Novak, 1940, 1952; Lomax and Anderson, 1941). Though the author's individual designation varies, in each the presence of a polypoid cystic hyperplasia has been associated with the development of an endometrial sarcoma. This makes 7 cases in all, including our own. The ages, in the 6 cases where this is given, have been rather young for uterine sarcoma, ranging from 28 to 52. Three cases (Stein, Novak, Lomax and Anderson) showed squamous metaplasia of glands or surface. In 3 (Froeschmann, Novak, Lomax and Anderson) there was a clear indication that the cystic hyperplasia preceded the sarcoma, as it probably just did in our case.

Such small numbers might suggest that the hyperplasia-sarcoma sequence is fortuitous, but this is partly offset by the intrinsic likelihood of a more organic connexion—an analogy with breast suggests itself. Moreover, the numbers increase if we widen the net to include such probable relatives of endometrial sarcoma as malignant stromatosis and mixed mesodermal sarcoma. The mural fibro-sarcomatosis uteri, associated with cystic hyperplasia, reported by Quirno and Schärer (1941), was probably malignant stromatosis; Park (1949) notes 3 instances of the same association. There have been 5 cases of corporeal mixed mesodermal sarcoma associated with or following an adenomatous or cystic hyperplasia (Gebhard, 1903; Hunzicker, 1908; Wolfe, 1932, case 2; Glass and Goldsmith, 1941; Schmidt and Schutz, 1948). In addition, 1 such case was found arising in an endometrial polypus (Herrera, 1949), and 1 occurred 2 years after the removal of an unusually large endometrial polypus (Amolsch, 1939). It is true that in most case reports of this tumour the condition of the endometrium is either not mentioned or is described as obliterated or atrophic, but it is possible that in some an initiating endometrial polypus has been destroyed by subsequent tumour growth. This is not a gratuitous suggestion but is prompted by the records of 7 mixed mesodermal or allied sarcomas associated with a few dilated or cystic glands such as might reflect such a background (von Franqué, 1899; Reid, 1902; Wiener, 1924; Durante and Roulland, 1924; Gamper, 1927; van Akkeren, 1930; Olinder, 1933). To these may be added a similar tumour reported by Lochrane (1933), discovered shortly after curettage had elicited polypoid curettings with large glands, and another, described by Wilson, Thornton and Nokes (1953), associated with an atrophic endometrium with cystic changes.

We have discussed these associations rather meticulously because, though they are too rare to have any practical importance, they may throw theoretical light on the old question of uterine carcino-sarcoma. For if cystic hyperplasia or polypi are sometimes pre-carcinomatous and rarely pre-sarcomatous it is clearly to be expected that both conditions will arise together occasionally from this common antecedent. This also is not gratuitous speculation but is distinctly suggested by the material. In 2 of the mixed mesodermal tumours cited (Glass and Goldsmith, 1941; Schmidt and Schutz, 1948) the associated hyperplasia has been quite atypical, and in 2 further cases (Wolfe, 1930; Clay, Evans and Snyder, 1952) the atypical hyperplasia was held by the authors to have reached definite malignancy, though the descriptions and pictures seem to us inconclusive. There are 10 cases of more definite carcino-sarcoma described in the literature with associated findings which support our suggestion. In 7 of these the sarcoma is of spindle cell or allied type with no aberrant differentiation, and therefore open to possible criticism as being misidentified anaplastic carcinoma. These 7 comprise: Spencer (1917), with an adeno-acanthoma, a spindle cell sarcoma, and 2

endometrial polypi, 1 of them with early sarcomatous change; Ritter (1925), with a myxofibrosarcoma, glandular hyperplasia, and atypical papillary areas interpreted as epithelial malignancy; Breiter (1938), with an adenocarcinoma, in part anaplastic, and a quite separate endometrial polyp with sarcomatous change in the stroma; Perry (1948, case 13), with coincident adenocarcinoma and fibrosarcoma 6 years after curettings had shown endometrial hyperplasia; Ahumada, Sammartino and Arrighi (1951), with a large endometrial polypus having partly the usual structure, partly adenocarcinoma, and partly spindle cell sarcoma; Martella (1952), with an endometrial polyp of usual structure passing over into adenocarcinoma, and an area of polymorphic sarcoma; Lisa, Pack and Gioia (1952), with an endometrial polyp showing both carcinomatous and sarcomatous change, together with an endometrium the description of which suggests retrogressed hyperplasia. In the remaining 3 cases the sarcoma was of mixed mesodermal type. These comprise: Läwen (1905), where it intermingled with an area of adenomatous hyperplasia passing into carcinoma; Nicholson (1918), associated with an adenoacanthoma and an endometrial polypus; Fels (1928), associated with endometrial hyperplasia and a quite separate adenocarcinoma. More doubtful evidence is offered by the cases of Jessup (1913), of mixed mesodermal tumour, "large irregular alveoli lined by cuboidal epithelium", and carcinoma; and those of Schröder and Hillejahn (1920) and Ehrlich (1942), which presented the combination of mixed mesodermal sarcoma, carcinoma and adenomyosis.

The term "carcino-sarcoma" has become something of a pathological solecism: it is also vague, but the linking of the two terms into a compound word must surely imply not only that both types of tumour are present but also that their association is not purely fortuitous. The suggestion that both can arise from a common pre-malignant antecedent was first made by Strong (1919). It accords with the fact that recorded uterine cases vary from quite separate tumours, through obvious "collision tumours", to cases approaching "composition tumours", as well as with the details we have given. It is not suggested, however, that all the peculiar and equivocal tumours of the uterus can be explained in this way.

Summary and Conclusions

A nullipara of 42, who had 2½ years irregular, later excessive, and eventually continuous bleeding, was found to have an endometrial sarcoma developing in a polypoid cystic hyperplasia. She has remained well for 3 years after operation. A comparison with similar and related cases in the literature suggests that endometrial hyperplasia and polypi may occasionally give rise to sarcoma, and that this may throw light on the genesis of uterine carcino-sarcoma.

We would like to thank Mr. J. D. S. Flew, under whose care this patient was admitted, for kindly allowing us to report this case.

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THE APPEARANCE OF LIPOID IN THE GENITAL TRACT OF THE IMMATURE FEMALE GUINEA-PIG

BY

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AND

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IN the mature guinea-pig lipoid is present in the lining epithelium of the uterine horns and distal part of the uterine body during the oestrous cycle, and is most intense during the period of activity of the corpus luteum (Nicol and Snell, 1954a, b). The lipoid is practically absent from the uterine horns about the time of implantation and occurs only in the epithelium of the lower cervix and vagina at oestrus. The lipoid can be produced experimentally in the lining epithelium of the genital tract of the ovariectomized guinea-pig by the injection of oestrogen and progesterone, and by varying the dose of these hormones the lipoid appearances present at the different stages of the oestrous cycle in the intact animal can be reproduced fairly accurately (Nicol and Snell, 1955). The above results suggest that the lipoid present in the epithelium of the uterine horns and distal part of the uterine body is an index of metabolic activity and depends on the balanced action of oestrogen and progesterone; in contrast the lipoid appearances in the epithelium of the lower cervix and vagina indicate a process of fatty degeneration which is under the control of oestrogen alone.

MATERIAL AND METHODS

The present research was carried out to ascertain when lipoid first appears in the lining epithelium of the genital tract of the young guinea-pig after birth. Sixteen guinea-pigs were used in this investigation and were killed at different ages. Two animals were killed at birth, 3 at 5 days old, 2 at 15 days old, 2 at 35 days old, 4 at 48 days old and 3 at 60 days old. The animals were killed with chloroform and the whole uterus and vagina were removed. All the specimens were fixed in 10 per cent formalin and frozen sections at 10 μ thick were made of the uterine horn, the upper and lower parts of the uterine body, the cervix and the vagina. The sections were stained with Sudan III for 15 minutes, then decolorized in 50 per cent alcohol and washed in distilled water. Haematin was used as a counterstain. High concentrations of alcohol were avoided as these may dissolve some of the lipoid (Kaufmann and Lehmann, 1929; Romeis, 1929).

RESULTS

The results are as follows: No lipoid was seen in the epithelium lining the genital tract of the animals killed at birth, 5 days old, 15 days old, 35 days old and 48 days old. In the 60-day old animals a moderate amount of lipoid is present in the epithelium. In the uterine horns and proximal part of the uterine body coarse lipoid globules are seen in the cells lining the mouths and ducts of the glands, and fine globules in the epithelium of the gland fundi. In the distal part of the uterine body a small amount of lipoid is present in the epithelium covering the villus-like processes, the globules being concentrated mainly in the infranuclear zone of the cells. In the lower part of the cervix and vagina the superficial cells contain a large amount of lipoid in the form of fine and coarse globules and many of the cells are in the process of being cast off into the lumen.

All the animals were examined daily and it was noted that the vaginal closure membrane had remained intact since birth. The external

genital organs of the 60-day old animals, however, showed signs of congestion.

Conclusions

The above results show that lipoid occurs in the lining epithelium of the genital tract of the guinea-pig before the oestrous cycle commences. This is in agreement with Bourg (1929) who reported that abundant fat is present in the uterine epithelium of the 6-day old mouse and with Alden (1947) who described the presence of lipoid in the uterine epithelium of rats aged 34 and 52 days. It is now known that the lipoid in the uterine epithelium of the mature animal is controlled by the balanced action of oestrogen and progesterone and that it disappears after ovariectomy (Snell and Nicol, 1955). It is also known that oestrogen alone can produce small amounts of lipoid in the uterine epithelium (Nicol, 1935), and this probably explains the appearance of lipoid in the 60-day old animals before oestrus has occurred; in fact, the congestion of the external genital organs and the vaginal appearances suggest that the first oestrus in these animals is about to commence.

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THE FUNCTIONAL ACTIVITY OF THE GENITAL TRACT IN POST-MENOPAUSAL ENDOMETRIAL CARCINOMA

BY

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THERE are two sharply contrasting views on the aetiology of endometrial carcinoma. It is maintained, on the one hand, that carcinoma develops in the body of the uterus irrespective of, and quite uninfluenced by, the state of the endometrium in which it arises. The alternative theory, supported by many observers on both clinical and pathological grounds, is that endometrial carcinoma is predisposed to by hyperplasia and polyps occurring in post-menopausal women, just as breast cancer is predisposed to by cystic dysplasia, and bowel cancer by polyps in the bowel mucosa. Since the nutrition and activity of the endometrium is largely governed by oestrogens, it has been inferred that the development of endometrial carcinoma is directly related to the long-continued action of oestrogen. In this connexion the close resemblance between the chemical formulae of naturally-occurring oestrogens and known carcinogenic compounds has been thought to be significant.

The apparently high incidence of endometrial carcinoma in cases of granulosa-cell and thecoma tumours of the ovary has given support to the view that oestrogenic activity, endometrial hyperplasia and carcinoma are closely related. On the other hand, in spite of the fact that oestrogens have been administered over a long period of time to a very large number of elderly women, only a few cases of carcinoma of the corpus following such therapy have been reported. Even where such a sequence was observed, the evidence of a direct causal relationship has been equivocal. A study of prior biopsies in cases of endometrial carcinoma has revealed the presence of hyperplasia in a number of cases, but follow-up studies of patients suffering from post-menopausal endometrial hyperplasia have shown that malignancy develops in only a small proportion of such cases.

If endometrial carcinoma results from continuing oestrogenic activity then one would expect to find evidence of the presence of oestrogen in abnormal amounts in the body of the post-menopausal women suffering from this condition. There has, until recently, been no satisfactory chemical method of estimating oestrogen in the body fluids in small amounts. It has been necessary therefore to have recourse to indirect methods. The presence of abnormal quantities of oestrogen in the body of a post-menopausal woman may be inferred from evidence of its stimulating action on the organs of the genital tract. I have studied the functional state of the pelvic organs in cases of endometrial carcinoma and I propose to report my findings and conclusions under the following headings:

(1) The uninvolved portion of the endometrium.
(2) The myometrium.
(3) The vagina, cervix and vulva.
(4) The Fallopian tubes.

STUDY OF THE UNINVOLVED ENDOMETRIUM

If, as has been suggested, endometrial carcinoma follows a long-continued action of oestrogen then it might be expected that the endometrium uninvolved by the malignant process would show evidence of some degree of oestrogenic stimulation, probably of the nature of hyperplasia. In many cases of carcinoma of the corpus the gross lesion seems localized, involving only a small area of the lining of the uterus. In this group are included a number of cases where the carcinoma is in the form of a

polyp. Under such circumstances it is frequently possible to study the adjacent but uninvolved endometrium.

Study of the uninvolved endometrium was possible in 56 out of 116 cases of endometrial carcinoma studied by me. In a number of cases the diagnosis was made from an examination of curettings, but for the most part the associated endometrium was obtained in hysterectomy specimens. For this purpose sections were prepared from the region of the junction between tumour tissue and the apparently normal endometrium.

In the great majority of cases the uninvolved endometrium showed an atrophic pattern. There were 25 cases of simple atrophy in which the mucosa was thin with relatively few, small glands in a fibrous stroma. On 16 further occasions there was a large proportion of cystic glands in an otherwise atrophic endometrium. The cells lining the large dilated glands were flattened and inactive in appearance. The stroma, which was scanty, had a loose, almost myxomatous arrangement with small spindle cells. To this inactive cystic, dilated gland pattern the term "cystic atrophy" has been applied. There were 10 examples of the association between a senile endometrial polyp of similar histological pattern and carcinoma. In 5 instances the associated endometrium was noted to be hyperplastic. In 3 of the cases this condition was characterized by an increased thickness of the endometrium, the glands showing a variation in size similar to that seen in "metropathia haemorrhagica". The glands were lined by columnar epithelium and the cells of both glands and stroma showed frequent mitotic figures. In the remaining 2 instances the hyperplasia took the form of an almost adenomatous arrangement of the glands. These findings are illustrated in Figures 1–4 and the percentage incidence is shown in Table I.

The literature contains many references to instances where endometrial hyperplasia was found simultaneously with adenocarcinoma. Indeed, much of the support for the theory linking endometrial hyperplasia, abnormal oestrogenic activity and carcinoma is derived from such reports. A critical study makes it clear that in many of the cases reported the discovery of hyperplasia and carcinoma was made when the patient was in the reproductive phase of life or actually at the time of the menopause (Hirst, 1929; Jones and Brewer, 1941). Indeed, in some instances the hyperplasia was diagnosed not long after puberty (Mazzola, 1938). The number of cases reported in which carcinoma was associated with hyperplastic changes in the endometrium after a definite cessation of menstruation is much smaller. Similar studies by a number of other investigators have suggested that in the great majority of cases the associated endometrium showed an atrophic pattern.

TABLE I

Incidence of Varying Patterns in the Uninvolved Endometrium Found in Association with Endometrial Carcinoma

Uninvolved Endometrium	Number of Cases	Percentage
Atrophic	25	44·6
Inactive dilated gland pattern—diffuse (cystic atrophy)	16	28·6
Inactive dilated gland pattern—localized (senile endometrial polyp) ..	10	18
Active hyperplasia	5	8·8

Meyer (1922) described the occurrence of islands of cancer in areas of endometrial hyperplasia in 4 cases and the description follows closely the appearance in 2 of the 5 cases in the present series. Taylor (1932) reported 4 cases of endometrial carcinoma found in association with "proliferative" changes in the endometrium. In 2 of the cases, however, he refers to the numerous, large, very thin-walled cystic glands which very strongly suggests that these represent the inactive cystic gland pattern to which further reference will be made. The most striking figures are given by Novak and Yui (1936), who, in a detailed study of the uninvolved endometrium, found it to be hyperplastic in no less than 40 per cent of cases. The diagnosis of hyperplasia in most of their cases was based on the finding of a "Swiss cheese" pattern of the glands. This interpretation was criticized by TeLinde (1936), who suggested that many of the specimens designated "hyperplasia" were in fact inactive. Certainly some of the photomicrographs illus-

trating the article show very large cystic dilated glands lined by a flattened inactive epithelium. Payne (1937) found the association of active hyperplasia and endometrial carcinoma in 4 out of 38 cases, an incidence of 10·5 per cent. This association was 5 times as common in the post-menopausal as in the pre-menopausal group, but they point out that fundal carcinoma is 3 to 4 times commoner in post-menopausal women. Morrin and Max (1939) reported associated hyperplasia in 17 out of 88 cases of endometrial carcinoma. Their cases however were not restricted to the post-menopausal years. Herrell (1939) disliked the use of the term "hyperplasia" referring instead to a "persistent proliferative pattern" with cystic dilatation of the glands. He attributed this to persistent oestrogenic activity and found this pattern in the uninvolved endometrium in 71 per cent of cases.

Jensen and Ostergaard (1954), in a study of 25 patients with endometrial carcinoma, were able to examine the uninvolved endometrium in 12 cases. Two cases showed simple atrophy, and there were 5 examples of endometrium showing inactive stroma and large cystic dilated glands lined with inactive epithelium. In 3 instances an endometrial polyp was present. The glands were lined by low inactive epithelium, and the stroma was fibrous. These last two categories were not considered to represent active hyperplasia which was, however, noted in the remaining 2 cases—an incidence of 16·6 per cent.

On the other hand, Cullen (1900) and Heurlin (1911) found the endometrium in association with endometrial carcinoma to be atrophic. The latter author, in a study of 44 cases, did not find any evidence of associated hyperplasia of the endometrium. The association of endometrial hyperplasia and carcinoma was noted only once in 23 cases by Fluhman and Stephenson (1929). Burch (1934) was adamant that he had never observed the uninvolved endometrium to be hyperplastic in cases of endometrial carcinoma occurring in post-menopausal women.

Jones and Brewer (1941) in a study of 49 cases of post-menopausal endometrial carcinoma found the endometrium to be atrophic except in a few instances. In some patients they noted that the endometrium was more stimulated than is usual in post-menopausal patients. The 2 cases of associated hyperplasia which they described occurred in pre-menopausal women.

Fahlund and Broders (1946), in a detailed article, described a study of uteri containing endometrial carcinoma and the uteri of normal post-menopausal women. They could not detect any difference in the average thickness of the endometrium in the two series. They found patterns other than simple atrophy in both the normal and in the uninvolved endometrium in cancer cases. But there was no increased incidence of proliferative endometrium in the latter group. Surprisingly, they found that in 41·8 per cent of cases of the uninvolved endometrium there was no cystic change in the glands, compared with 20 per cent in the normal series. The incidence of endometrial polyps in the normal was 22 per cent, and 4·7 per cent in the uteri with fundal carcinoma.

There is frequent reference in the literature to the association between endometrial polyps and carcinoma. This is briefly summarized in the accompanying table.

Author	Date	Association of Polypi and Carcinoma (Per cent)
Stacy	1929	7·5
Beattie	1933	4
Scheffey *et al.*	1943	7·8
Barns	1942	5·3
Hertig and Sommers ..	1949	12
Way	1954	26·6

Hirson (1939) described 4 cases, Alfieri (1940) 1 such case, and Jensen and Ostergaard (1954) 3 cases out of 12 cases investigated.

The term "polyp" is a macroscopic rather than a histological one, referring simply to a growth which is attached by a pedicle. In many of the reports in the literature there is no accurate histological description of the polyp. It seems preferable to consider the polyp on the basis of its histology. Thus a sharp distinction is drawn between the solitary senile endometrial polyp which is found in association with an atrophic

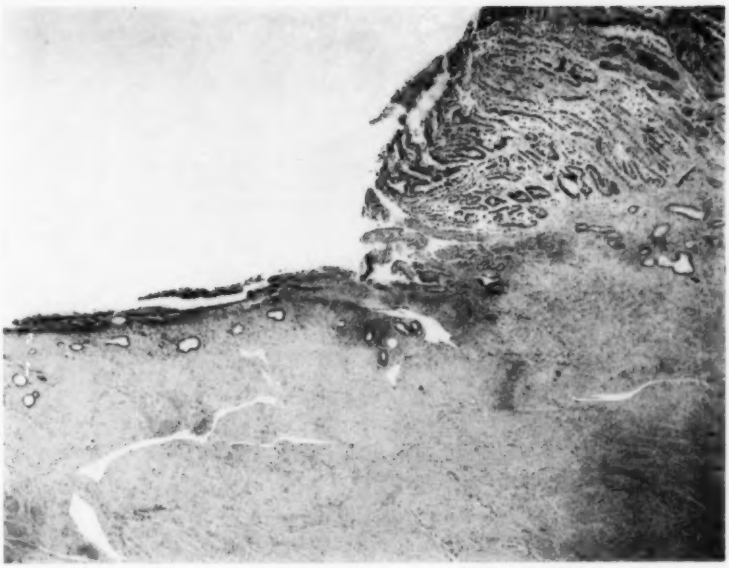

FIG. 1

Endometrial carcinoma associated with atrophy. H. & E. ×22.

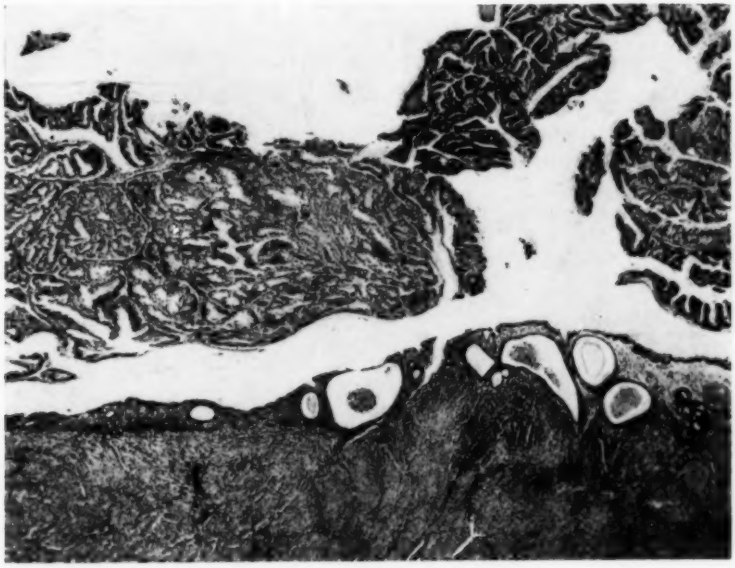

FIG. 2

Endometrial carcinoma associated with inactive dilated gland pattern diffuse. H. & E. ×27.

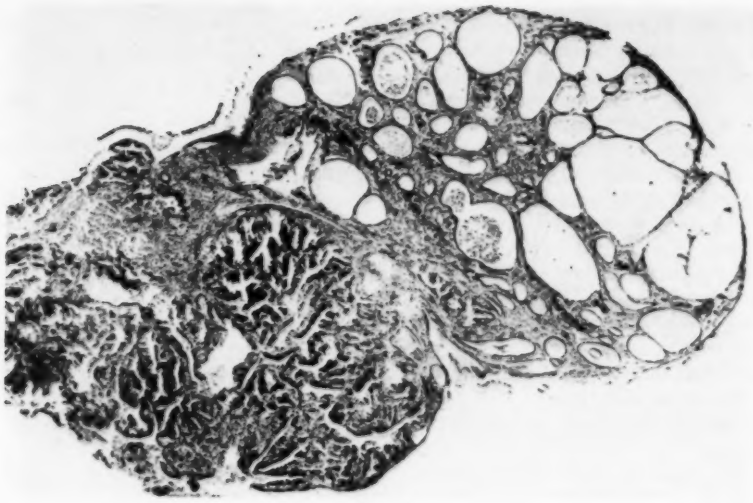

FIG. 3

Association of carcinoma and senile endometrial polyp. H. & E. ×20.

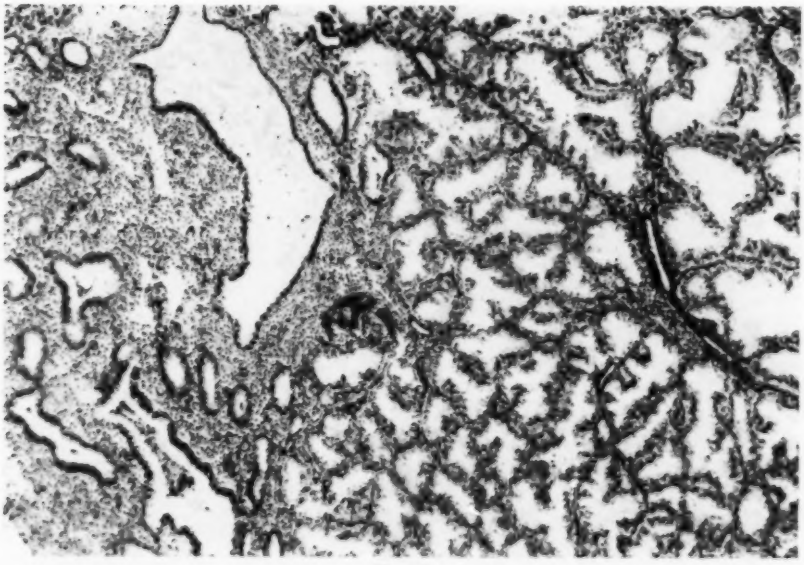

FIG. 4

Adenocarcinoma associated with active endometrial hyperplasia. H. & E. ×50.

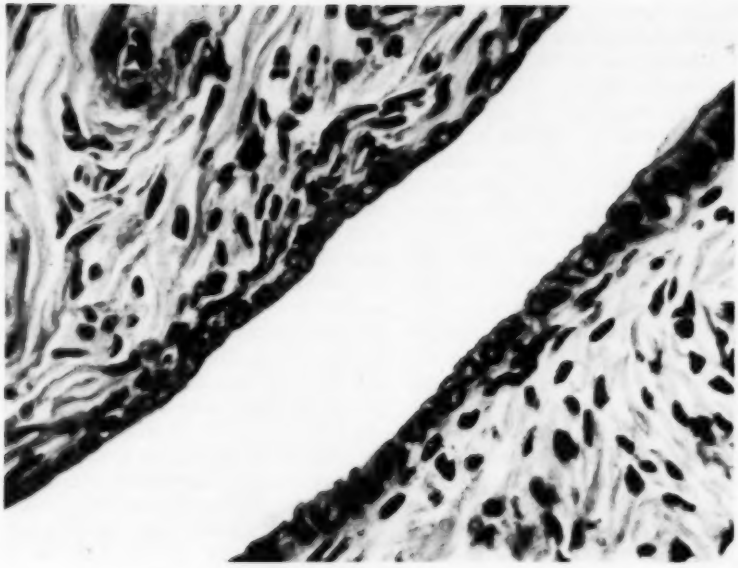

FIG. 5

Atrophy of endo-salpinx in endometrial carcinoma. H. & E. ×680.

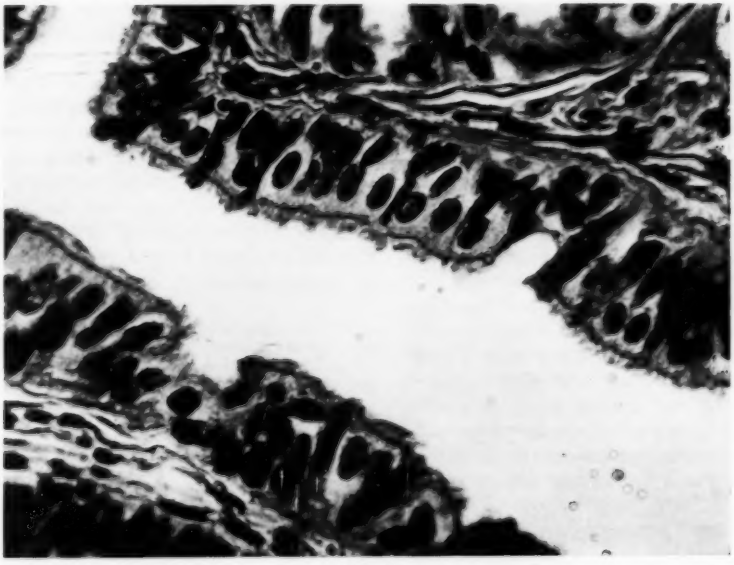

FIG. 6

Hyperplasia of endo-salpinx in post-menopausal patient with a granulosa cell tumour of the ovary. H. & E. ×680.

endometrium, and those cases where the whole of the endometrium is thickened and polypoidal as in many cases of active hyperplasia.

Some explanation must be sought for the diverse findings which have been reported. In my opinion part of the explanation is that some of these observers have studied the abnormal more than the normal, and have accepted the conventional view that the senile endometrium always shows a simple atrophic pattern. In a previous paper (McBride, 1954) I have emphasized that this is not so, simple atrophy of the endometrium being present in only about 60 per cent of normal post-menopausal women. Cystic atrophy was present diffusely throughout the endometrium in an additional 20 per cent of cases. This pattern was characterized by disparity in gland size and by an inactive appearance of the flattened cells lining the glands and of the stromal cells. In a further 15 per cent of the total, senile endometrial polypi of similar histological pattern, and associated with simple or cystic atrophy of the remainder of the endometrium, were present. There was no clinical or histological evidence to suggest that these were examples of local hyperplasia as has been asserted. However, activity of the endometrium, either a frank hyperplasia or a proliferative pattern, was noted in about 5 per cent of asymptomatic post-menopausal women. Active hyperplasia was of the cystic glandular variety or, less commonly, of an adenomatous pattern, the glands being closely packed together with little intervening stroma. The majority of such cases were observed in the early post-menopausal years. The percentage incidence of these histological findings is shown in Table II.

It will be seen that carcinoma occurs in association with all these endometrial patterns, and before it can be claimed that carcinoma is predisposed to by any particular state it must be shown that this special state exists much more frequently in the uninvolved endometrium in cases of carcinoma than it does in the normal woman.

TABLE II

Incidence of Varying Endometrial Patterns Found in the Normal Post-menopausal Woman

Endometrial Pattern	Percentage Incidence
Atrophic	60 (approx.)
Inactive dilated gland pattern—diffuse (cystic atrophy)	20
Inactive dilated gland pattern—localized (senile endometrial polyp) ..	15
Active (hyperplasia or proliferative)	5 (approx.)

In most senile endometriums an occasional cystic gland is found. When the proportion of dilated glands reaches a certain level the endometrium falls into the category of "inactive dilated gland pattern"—either polypoid or diffuse. I have previously produced arguments to suggest that this pattern should be considered as a variant of an atrophic endometrium. At first sight it may seem incongruous to suggest that a polyp may be an example of atrophy. But transitional forms from simple to cystic atrophy are frequently seen. Moreover the association of a senile polyp with either simple or cystic atrophy of the rest of the endometrium is common. These variations in the proportion of cystic dilated glands are noted in the normal and in the uninvolved endometrium and it is sometimes difficult to decide whether a particular endometrium should be classified as "atrophic" or the "diffuse inactive dilated gland pattern".

If simple atrophy, cystic atrophy and senile endometrial polyps are grouped as examples of inactivity of the endometrium then the figures for the normal and the uninvolved endometrium are 95 per cent and 91·2 per cent respectively. Thus associated hyperplasia and carcinoma of the endometrium occurs in 8·8 per cent of cases. This figure loses much of its significance when it is remembered that active hyperplasia and proliferation can occur in the endometrium of the normal post-menopausal woman. The incidence is in the region of 5 per cent during the first 5 years after the menopause—falling sharply after that time. The number of cases (5) is too small for the figures in the individual age groups to be significant, but it does not seem that cystic glandular hyperplasia and endometrial carcinoma are particularly concurrent.

It is difficult to reconcile this finding with the reports in the literature that hyperplasia was found in the uninvolved endometrium in 40 per cent of cases. However, there are no absolute criteria for the diagnosis of endometrial hyper-

plasia, and difficulty may be encountered in deciding where the border line is to be drawn between a senile endometrium with dilated glands and endometrial hyperplasia. Mere disparity of gland size giving a "Swiss cheese" pattern is not sufficient to justify a diagnosis of active hyperplasia. The superficial resemblance to hyperplasia is belied by the inactive histological appearance of the flattened cells lining the dilated glands, and the sparse stroma. I have referred to TeLinde's criticism of the criteria adopted by Novak and Yui. Following their paper he studied the normal post-menopausal endometrium in his own laboratory. In 55 per cent of cases he found the same histological picture which Novak and Yui had interpreted as hyperplasia. This caused him to question the aetiological significance of the incidence of 40 per cent hyperplasia in the carcinoma group referred to above. It is of further interest to record that 5 years later Novak, in conjunction with Richardson, found an active endometrium in 25 per cent of post-menopausal women who were not suffering from bleeding. It has been stated that different histological characteristics have been adopted between hyperplasia of the reproductive age and that appearing after the menopause, and it is suggested that the criteria used for post-menopausal hyperplasia are more liberal.

In only one other paper (Fahlund and Broders, 1946) is there a combined study of the uninvolved endometrium and the normal post-menopausal endometrium by the same observers. And in this investigation the endometrial patterns noted in the two series occurred in nearly the same proportions. There was no increase of hyperplasia or activity of the endometrium in the patients with carcinoma. I feel that where other observers have reported a high incidence of hyperplasia in the uninvolved endometrium they have not taken into account the fact that a cystic gland pattern—bearing a superficial resemblance to hyperplasia—is a frequent finding in the endometrium of the normal asymptomatic post-menopausal woman.

The Myometrium

I have been impressed by the frequent occurrence of endometrial carcinoma in the small atrophic uterus, and the diagnostic pitfalls, and technical difficulties of hysterectomy in such cases are known to all gynaecologists. It seems, therefore, that information will be gained from an assessment of the condition of the uterus in which carcinoma occurs in the elderly woman.

Sixty-four uteri removed because of endometrial carcinoma were examined and classified as follows. A uterus was considered to be atrophic when its length was 2½ inches or less in a parous woman, or 2 inches or less in a patient who had not borne children. The results are shown in Table III.

Table III

Condition of the Uterus in Post-menopausal Patients Suffering from Endometrial Carcinoma

State of Uterus	Number of Cases	Percentage
Atrophic	29	45·3
Normal	10	15·6
Enlarged (due to tumour) ..	13	20·3
Enlarged (due to fibroids) ..	12	18·8

In the literature authors do not as a rule distinguish between pre- and post-menopausal patients and the following figures are not strictly comparable. Healy and Brown (1939) found the uterus was not enlarged in 22 per cent of cases and in almost half of the total the uterus, although enlarged, was not over the size of a 2½-months pregnancy. Miller (1940) noted that the uterus was not enlarged in 31 per cent of cases of endometrial carcinoma. Enlargement of the uterus was found in 69·4 per cent of cases by Cosbie and Henderson (1939) and in 63 per cent by Barns (1942).

In my own series, dealing solely with cases occurring after the menopause, an atrophic uterus was noted in 45·3 per cent of cases. Enlargement of the uterus, not due to the presence of co-existing fibroids was present in 20·3 per cent of the total. In many of these cases the enlargement of the uterus was due in part to the actual tumour growth. The enlargement was not apparently due to myometrial hyperplasia as in many cases the walls of the uterus were a quarter of an inch thick or less. Under such circumstances it is not possible to

determine whether or not atrophy has occurred. In 15·6 per cent of cases, classified as being normal in size, there was evidence of lack of atrophic change, though in a proportion of these cases the patient was in the early post-menopausal years at the time of the hysterectomy.

Enlargement of the uterus due to the presence of co-existing fibroids was recorded in 18·8 per cent of patients. There is frequent reference in the literature to the common association between endometrial carcinoma and uterine fibroids. Indeed, when post-menopausal bleeding occurs from a uterus which is enlarged by fibroids, the possibility of a corpus carcinoma is uppermost in the clinician's mind. Norris and Dunne (1936) found uterine fibroids in 35 per cent of patients with endometrial carcinoma and it has been suggested that the two conditions may have a common aetiological factor. The following figures have been given by the different authors:

Healy and Brown (1939)	38·0 per cent
Miller (1940)	19·8 per cent
Barns (1942)	25·3 per cent
Scheffey *et al.* (1943)	23·5 per cent

The finding of fibroids in a uterus does not, however, prove conclusively that atrophy has not occurred. This was apparent in several of the cases investigated in this series. One uterus measured only 2 inches in length but had attached to it a large pedunculated fibroid showing extensive degenerative change. In another instance the fibroid, also of considerable size, was calcified. Moreover in a number of cases small seedling fibroids were present in uteri whose cavity measured 1 inch or less.

The uterine fibroid is a common tumour, occurring in 15 per cent of all women over 30 years according to autopsy reports. It would be strange if it were not often co-existent with endometrial carcinoma, and the association may well be fortuitous. There is as yet no conclusive evidence that fibroids are a result of excessive or abnormal oestrogenic activity. Moreover fibroids grow actively during the reproductive years and commonly retrogress after the menopause. Indeed it was noteworthy that extensive degeneration had occurred in the fibroids found in many of the uteri examined in this series.

It would seem that the frequency of atrophy of the uterus, as well as that of enlargement of the uterus due to fibroids, in cases of endometrial carcinoma is similar to that found in normal post-menopausal women. There was no evidence to suggest that the enlargement of the uterus which has frequently been noted is due to hyperplasia of the myometrium similar to that seen in association with "metropathia haemorrhagica".

State of Nutrition of the Vagina

In a study of the state of nutrition of the vagina it seemed that clinical impressions were not sufficiently accurate and that they were too personal to permit of firm conclusions being drawn. Therefore, in addition to clinical examination, recourse was had to the staining of vaginal smears by Schor's method and the iodine test for glycogen in the vaginal mucosa.

Clinical Observations

In the elderly woman the vaginal mucosa commonly has a smooth, dry and glistening appearance as a result of the loss of the normal rugae and thinning of the squamous epithelium. Progressive atrophy even to a single layer of cells may occur but the condition is normally asymptomatic. However, because of its atrophic condition, the vaginal epithelium is easily traumatized and is less resistant to infection. In senile vaginitis, examination reveals numerous small punctate superficial bleeding areas which may become fused together, and in the later stages adhesions frequently follow as a result of apposition of the vaginal walls. The condition is mostly confined to the upper two-thirds of the vagina and the vaginal aspect of the cervix.

There are few references in the literature to the state of nutrition of the vulva and vagina, or the activity of cervical secretion in cases of endometrial carcinoma, three quarters of which cases occur after the menopause. The association of senile vaginitis and endometrial carcinoma has been reported by Anspach (1936) in 1 case, and Cosbie and Henderson (1939) in 2 cases. On the other hand Randall (1945) was impressed by the frequency with which elderly women with adenocarcinoma of the corpus

showed a surprisingly well preserved vaginal wall. He considered that endometrial carcinoma did not develop in the woman having hot flushes, with atrophic changes in the vulval and vaginal tissues, and with no evidence of oestrogen effect on the endometrium and uterus. Corscaden (1951) agreed with this view and stated more specifically that he had not found endometrial carcinoma in a woman who at the same time showed an atrophic or senile vaginitis. According to these authors the vagina in patients with corpus carcinoma had a more youthful appearance than one would expect in women well past the menopause. There was apparently less atrophy, less pallor and thinning of the mucosa.

In a series of 116 cases of endometrial carcinoma studied by the present writer an atrophic vaginitis was present in 22 cases, an incidence of 18·9 per cent. In 4 instances the condition was so advanced as to be termed adhesive vaginitis.

Apart from the scientific importance of this association there is considerable clinical significance which is well illustrated by the following 3 case histories.

Case No. 1. This patient, when 22 years past the menopause, was curetted because of post-menopausal bleeding, and a senile endometrial polyp with inactive cystic glands was removed. Twelve years later she complained of further bleeding and a diagnostic curettage was indicated. The vagina and vaginal aspect of the cervix showed an atrophic vaginitis with many minute punctate haemorrhages. When the uterine sound was passed through the cervical canal, the fundus of the uterus was perforated and the curettage was abandoned. It was considered apparently that the vaginitis was sufficient to account for the bleeding of which she complained, and the patient was dismissed from hospital. This patient came under my care 3 months later when she was admitted to the Royal Samaritan Hospital for Women. Bulky curettings were obtained on curettage and histological examination confirmed the diagnosis of endometrial carcinoma.

Case No. 2. In this case the correct diagnosis was delayed for 3 years because the intense vaginitis, complicated by vaginal adhesions, was regarded as the source of the post-menopausal bleeding. On 2 occasions attempted curettage had been abandoned because of difficulty in locating the cicatrized cervix due to the numerous and extensive adhesions.

Case No. 3. A nulliparous diabetic patient, who had previously been treated for pruritus due to a diabetic vulvitis, was admitted to hospital 20 years after the menopause because of bleeding. A senile vaginitis was present and I had considerable difficulty in locating the canal in a small atrophic cervix. A reasonable explanation for the bleeding was obviously present. However, eventually a fine probe was passed into the cervical canal and dilatation carried out. Bulky friable curettings were obtained from the fundus of the uterus and histological examination revealed endometrial carcinoma.

These cases reinforce Anspach's (1936) warning that in all cases of senile vaginitis it is of utmost importance to establish the correct diagnosis, and to rule out very carefully the possible presence of a malignant condition.

Vaginal Smear and Oestrogen Activity

In order to assess the physiological atrophy of the vagina a study was made by me in cases of endometrial carcinoma of vaginal smears stained by Schor's method. Where marked oestrogen deficiency is present all the cells are from the basal layer of the vaginal wall and leucocytes are numerous. Slight oestrogen effect is manifested by the presence of cells from the superficial vaginal layer, the cytoplasm of the cells being basophilic. When there is moderate oestrogen effect the predominant cells become acidophilic and cornification is occasionally present. High cornification in a post-menopausal woman is suggestive of disordered oestrogenic activity and is frequently associated with endometrial hyperplasia.

Oestrogen deficiency was present in 61·5 per cent of the cases examined and slight oestrogen effect was found in 30·8 per cent of the total. Moderate oestrogenic effect was noted in 7·7 per cent of patients, but there was not a single instance in which the oestrogen effect could be termed "marked". In no case was there cornification of the vaginal cells comparable to that found in patients known to be receiving oestrogen therapy, or in a patient who had a granulosa-cell tumour of the ovary. These findings are contrary to previous reports of Ayre and Bauld (1946) and Dockerty and Mussey (1951) that vaginal smears of women with endometrial carcinoma showed evidence of high activity of endogenous oestrogen.

Glycogen Content of Vaginal Mucosa

For the purposes of comparison the corresponding figures obtained by Mack (1943) for

normal post-menopausal women are given in Table IV. From a study of the table it would

TABLE IV

State of Nutrition of Vagina in Normal Post-menopausal Women and in Patients Suffering from Endometrial Carcinoma

	Advanced Oestrogen Deficiency Per-centage	Slight Oestrogen Effect Per-centage	Moderate Oestrogen Effect Per-centage
Normal post-menopausal women	70	27·6	2·3
Post-menopausal patients with endometrial carcinoma	61·5	30·8	7·7

appear that some evidence of oestrogenic activity is present in less than 40 per cent of patients with endometrial carcinoma. This figure loses much of its apparent significance when it is realized that similar evidence of activity has been observed in 30 per cent of normal post-menopausal women. It does not appear from this that physiological atrophy of the vagina is appreciably less frequent in patients with endometrial carcinoma, or conversely that there is evidence of abnormal oestrogenic stimulation of the vagina in patients who have developed endometrial carcinoma.

I have on several occasions noted a youthful condition of the vagina and cervix in post-menopausal patients, but not once in a case where endometrial carcinoma was present. I will refer to 6 examples where the appearances were very striking. Twice the condition was present in patients who were receiving oestrogen therapy. In the first oestrogen had been administered orally in the form of stilboestrol for a period of over 2 years, and hyperplasia of the endometrium was also present. The other patient had been using "Menopax" ointment locally in the treatment of pruritus vulvae. There was 1 example of a youthful appearance of the vagina in a patient who was later found to have a granulosa cell tumour of the ovary. In the other 3 instances not only were the vaginal walls healthy, but there was abundant secretion of mucus from the cervix. All these 3 patients had an associated hyperplasia of the endometrium. In 2 of the cases the conditions were observed in the same patient at intervals of 5 and 8 years respectively, the patients' ages being 75 and 72 years at the time of the original observations.

I have not found it possible to assess atrophy of the external genitalia or of the cervix so accurately, and am unable to express the findings numerically. But reference is made in our records of patients with endometrial carcinoma to the presence of atrophic vulvitis. Atrophy of the cervix, which in some cases was noted to be flush with the vaginal vault, is occasionally noted. This supports the findings of Cosbie and Henderson (1939) that, in 38 cases of corpus carcinoma, the cervix was atrophic in 6 instances and "catarrhal" in a further 6. I have not personally observed active secretion of mucus from the cervix in a post-menopausal woman whose uterus contained a carcinoma. As I stated in the previous paragraph this phenomenon has, however, been observed by me in post-menopausal patients who have been receiving oestrogenic therapy, patients with granulosa cell tumours and with associated endometrial hyperplasia.

Thus a study of the vagina in patients past the menopause shows that some oestrogen effect is present in almost 30 per cent of cases. It is not surprising therefore to report a lack of atrophy of the vagina in 40 per cent of patients with endometrial carcinoma. The incidence of physiological atrophy in such cases is only slightly less than that of normal post-menopausal women. Further, under the influence of oestrogen the vulva and vagina have a more youthful appearance, the vagina becomes rugose and its cells contain glycogen. Moreover the cervix is succulent and frequently shows active secretion of mucus. Such conditions which are found in the post-menopausal woman when an excess of oestrogen is present are noticeably absent in patients with endometrial carcinoma.

THE FALLOPIAN TUBE

In common with other genital tract tissues the Fallopian tube undergoes atrophic changes after the menopause. Voinot (1900), in a study of the

Fallopian tubes of senile women, found that the epithelium became cuboidal or flattened, except in the interstitial part where it remained columnar. He noted that cilia were sometimes retained even when the epithelium became flattened. This was confirmed by Hoehne (1908) who was able to demonstrate cilia in the Fallopian tube of a woman of 60, 12 years past the menopause. Tröscher (1917) and Novak and Everett (1928) agreed that conspicuous atrophic changes were not seen except in the Fallopian tubes of women of 60 or over. They observed that the epithelium was little changed for a considerable time, later becoming cuboidal or flat. Siddal (1943) stressed the changes in the connective tissue of the folds which showed an increase in fibrillar elements and became less cellular. The folds became broader and plumper and tended to lose their convolutions.

Novak and Everett (1928) found that in endometrial hyperplasia associated with functional bleeding the epithelium of the Fallopian tube was tall and narrow. Cilia were relatively abundant and well marked while the non-ciliated cells, though clearly differentiated, showed no sign of secretory activity. Hyperplasia of the Fallopian tube in patients who had feminizing tumours of the ovary was noted by Tietze (1932).

It would seem that, even where an excess of oestrogen is present, the local tissues may remain atrophic and inactive by reason of a lack of responsiveness. For this reason a study was first made of the Fallopian tubes of post-menopausal women in whom a definite excess of oestrogen was present. That the epithelium of the Fallopian tubes is responsive to oestrogens in the post-menopausal era is seen by the occurrence of hyperplasia of the endo-salpinx in patients with a granulosa cell tumour of the ovary. This finding is illustrated in Figure 6. The ciliated cells are both tall and broad, measuring often as much as 40 microns in height, and 12 microns in breadth. The nucleus is large and either round or slightly ovoid. It is situated far above the basement membrane, often near the ciliated end of the cell. The nuclei of the secretory cells are much more deeply placed near the basement membrane. This gives the impression of a double layer of nuclei. The folds are numerous and the connective tissue is cellular. These findings were present in 4 cases where a feminizing tumour of the ovary was present and in 2 cases of post-menopausal endometrial hyperplasia.

The Fallopian tubes were examined by me in 34 cases of endometrial carcinoma occurring in post-menopausal women. These patients were from 2 to 25 years after the menopause. In 31 cases atrophy of the tubes was present. The atrophic changes were reflected both in the flattening of the epithelium and the sclerotic changes in the folds. There were 3 instances where atrophic changes had not occurred. These patients were 4, 5 and 8 years past the menopause. At the same time extreme degrees of atrophy of the tube were frequently noted in the early post-menopausal years. In no case was hyperplasia of the endo-salpinx, similar to that met with in granulosa cell tumours of the ovary and endometrial hyperplasia, encountered.

Thus evidence of abnormal oestrogenic stimulation of the Fallopian tube was conspicuously absent in this study of patients with endometrial carcinoma.

It was not possible in every case of endometrial carcinoma to correlate the functional activity of the different parts of the genital tract. But simple atrophy, cystic atrophy of the endometrium, and senile polypi were invariably found in association with atrophic changes in the Fallopian tube and cervix. Further the frequent association of senile vaginitis and an atrophic uterus in such cases was confirmed.

Discussion

It has been my purpose in this investigation to make reference to the atrophic processes which occur in the genital tract of the normal ageing woman. I have emphasized, with particular reference to the vagina and the Fallopian tube, that even some years after the menopause atrophic changes are not invariably present, and that evidence of some oestrogenic activity may be present in these tissues in the asymptomatic post-menopausal woman. The possible variations in the post-menopausal endometrial pattern have been considered in detail, and the fact that this structure may contain cystic

dilated glands under normal circumstances has been stressed. Moreover I have indicated that a superficial resemblance of this pattern to cystic glandular hyperplasia may cause confusion, and may erroneously be interpreted as indicating abnormal oestrogenic activity at this time.

The action of oestrogen in producing hypertrophy of the vagina, secretion from the cervix and endometrial hyperplasia in the post-menopausal patient is well-established. Support for this view has been provided in the present study. Moreover presumptive evidence to show that hyperplasia of the endo-salpinx in the elderly woman occurs under the influence of oestrogens has been produced.

From a study of the genital tract in the post-menopausal woman suffering from endometrial carcinoma it would seem that the various organs show the same degree of atrophy as that found in the normal elderly woman. There is no evidence of an increased incidence of hyperplasia of the epithelia which have been shown to be responsive in the post-menopausal era to the action of oestrogens.

These facts, however, are not claimed to discredit the theory of an aetiological connexion between oestrogenic activity and endometrial carcinoma. Several explanations of these findings are possible. It may be that endometrial carcinoma results from disordered oestrogenic metabolism in a form which does not stimulate physiological growth and hyperplasia of the Müllerian duct tissues. Alternatively any hypothetical excess of oestrogen in the woman's body may be entirely consumed by the carcinoma in its metabolism, leading to an actual deprivation of oestrogen to the other tissues of the genital tract. These are merely speculations, and further and more accurate biochemical studies of oestrogen and its metabolites in the normal post-menopausal woman, and in patients suffering from carcinoma will perhaps throw some light on the subject.

On the other hand considerable stress has always been placed on the length of time a carcinogenic stimulus requires to act before inducing malignant change. It may be that oestrogens are in fact a cause of endometrial carcinoma but that their action—the production of endometrial hyperplasia—is exerted some years before the development of the malignant condition. This influence might conceivably occur during the reproductive life or about the time of the menopause when anovulatory cycles and cystic glandular hyperplasia are more common. A follow-up of conditions at that time thought to be associated with hyper-oestrinism, e.g., "metropathia haemorrhagica" might clarify this point.

The importance of hereditary and genetic factors in the development of malignant disease does not require to be stressed here. Reference must however be made to the metabolic abnormalities commonly seen in patients with endometrial carcinoma. Way has drawn attention to the frequency with which such patients show adiposity and glycosuria. It is perhaps significant that these disturbances have in all probability an endocrinological basis.

With such a wide field of investigation available I have restricted myself in the present paper to a very limited objective. In this study, clinical and laboratory, of patients with endometrial carcinoma, I have not found evidence of an altered functional state in comparison with normal elderly women. In particular there is no evidence, admittedly of an indirect nature, that in the malignant cases there is continuing excessive stimulation by oestrogens of the different organs of the genital tract. Further, support for a close aetiological relationship between oestrogenic activity, hyperplasia and endometrial carcinoma is not, as has been claimed, to be found in a study of the functional state of the utero-vaginal tract in patients with endometrial carcinoma.

Summary

(1) The patterns of the uninvolved endometrium in carcinoma cases are the same as in normal women, and the incidence of hyperplasia and proliferation in the uninvolved endometrium is only slightly higher than in the normal.

(2) Atrophic changes in the uterus of normal patients and patients with carcinoma are approximately equal. The incidence of fibroids is not increased in patients with carcinoma.

(3) The incidence of physiological atrophy of

the vagina in patients with endometrial carcinoma is not significantly less than in normal elderly women.

(4) The association of a senile vaginitis with 18·9 per cent of cases of endometrial carcinoma is reported, and the clinical and scientific importance of this finding is elaborated.

(5) Evidence of the responsiveness of the endo-salpinx to oestrogenic stimulation in the post-menopausal woman is provided by a study of patients with granulosa cell tumours of the ovary.

Atrophic changes in the Fallopian tube in patients with endometrial carcinoma are parallel to those in normal elderly women.

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INTRA-UTERINE PASTES FOR THERAPEUTIC ABORTION

BY

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THE use of intra-uterine pastes for the induction of therapeutic abortion began in Europe, spread to America, and from enquiries we have made is now the method of choice in certain centres in Britain. The introduction of these pastes originated as an easy alternative to the more difficult, and sometimes dangerous, method of dilatation of the cervix by laminaria tents, or the more direct method of dilatation and immediate evacuation of the products of conception. This method had, for these reasons, been used on 32 occasions at this hospital in the last 4 years.

The first 21 of these cases were uneventful apart from 2 cases who returned 1 month and 2 months later respectively, with bleeding per vaginam. Dilatation and curettage in both cases, however, showed retained products of conception. The 22nd case developed transient haemoglobinuria and very mild jaundice but no constitutional upset and rapid recovery. The 23rd and 24th cases were complicated by pelvic infection and the 28th case (Case B) is reviewed later. The 29th case developed a pulmonary embolus on the 6th day which was probably unconnected with the method of induction and from which she recovered. The complications of the 32nd case (Case A), however, whose case history is given below, finally decided us to abandon this method. Complications such as we describe have not, to our knowledge, been reported as a consequence of this method in this country.

CASE REPORTS

Case A. Mrs. J.L., aged 22 years, a primigravida, was admitted to hospital on 16th March, 1954, when she was 12-weeks pregnant. Termination of this pregnancy had been advised by a chest physician because she had had a right pneumonectomy performed in October, 1952 for tuberculosis. Her general condition was good. Clinical examination indicated that the left lung was normal, and a radiological examination, which had been carried out on 22nd February, 1954, also showed a normal appearance of the left lung.

On 17th March, 1954, 15 c.cm. of Utus paste was injected slowly into the uterine cavity under general anaesthesia. The time taken for the injection was 5 minutes. Within 10 minutes of this injection, as the patient was coming round from the anaesthetic, she became cyanosed, and her pulse rate rose to 120 per minute. Her airway was confirmed as clear. Continuous oxygen was commenced, but her profound cyanosis, dyspnoea, and tachycardia persisted. Bedside radiograph of chest showed "right thoracoplasty with faint mottling in the left lung field". Oxygen therapy was continued, but despite this, her symptoms persisted. The next day her condition was unchanged. There were no added sounds in the left upper lobe, but the lower lobe was the site of fine inspiratory râles with good air entry and no broncho-spasm. A chest X-ray showed "many ill-defined opacities in the left lung field with a tendency to confluence, densest in the perihilar region. Less opacity in the peripheral region. The apical area is completely clear. Appearances highly suggestive of pulmonary oedema." Slight icterus was detected in her conjunctivae and the urine was of a dark red colour. Blood examinations gave the following results: haemoglobin 89 per cent; red cells 5,230,000 per c.mm.; white cells 29,200 per c.mm.; blood urea 52 mg. per cent; serum alkaline phosphatase 4 units per cent; serum proteins 5·75 g. per cent; serum bilirubin 0·4 mg. per cent. Liver function tests were normal. Oxyhaemoglobin bands were shown in the serum by spectroscopic examination. Examination of her urine showed: reaction, acid; albumen, large amounts; scanty pus cells and debris. Culture showed a heavy growth of *Bacterium coli.* The presence of oxyhaemoglobin was confirmed. An electrocardiogram showed "sinus tachycardia. Right ventricular strain with P. pulmonale."

She was treated with alkalies by mouth, Penicillin systemically and morphia gr. 1/6th 8-hourly. Continuous

oxygen was given by B.L.B. mask. On the second and third days after operation her condition remained essentially unchanged. The oxyhaemoglobin, however, decreased in her urine, the output of which was within normal limits. Her X-ray on the third day showed "great regression of the appearances with complete clearance in the peripheral regions". The foetus was passed 72 hours after operation. She slowly recovered, and oxygen inhalation was discontinued 5 days after operation, when X-ray appearances showed "left lung now clear with complete disappearance of the previous opacities". Her urine had, by then, returned to normal. The remainder of the products were spontaneously passed on 30th March, 1954. An electrocardiogram taken on 25th March, 1954, showed "sinus tachycardia and ventricular premature beats and 'summation beats'. The tracing was consistent with right ventricular stress, rotation of the heart clockwise and anoxic myocardial changes."

The patient was discharged on 10th April, 1954. Vaginal examination showed that the uterus was normal in size and mobility. There were no adnexal swellings and no tenderness was elicited. She was seen again on 12th May, 1954. Her general condition was good, with no dyspnoea on exertion. Pelvic examination was normal, and a chest X-ray showed "left lung completely clear". Her electrocardiogram showed "sinus tachycardia; slight R. axis deviation. Pattern is still abnormal and suggestive of right ventricular stress and probably some pulmonary hypertension."

Summary. A case of pulmonary oedema with intravascular haemolysis and haemoglobinuria following the use of intra-uterine paste. The pulmonary oedema was an especially grave complication in view of the previous pneumonectomy and produced serious cardio-respiratory embarrassment.

Case B. Mrs. N.D., aged 29 years, was admitted to hospital on 1st May, 1953. She had 2 children and was a known case of bronchiectasis and mild, benign hypertension. She was 14-weeks pregnant with a history of an attack of Rubella one month prior to admission. She was given a prophylactic course of Estopen for 5 days after admission, together with postural drainage to help clear her bronchiectasis. Her urine was sterile and contained no albumen, cells or casts. Her blood pressure was 150/100 mm./Hg. On 16th May, 1953, 15 c.cm. of Utus paste was injected into the uterine cavity under general anaesthesia. The time taken for the injection was 5 minutes. Thirty hours later the foetus and placenta were passed with minimal blood loss. This was followed by a rigor, copious vomiting, pain over an enlarged liver, and collapse with systolic blood pressure of 65 mm. Hg. Under appropriate treatment, she slowly recovered over 24 hours, with the blood pressure rising to 95 mm. Hg. Slight icterus was then present. Blood examination showed a total white count of 59,600 per c.mm. with 95 per cent polymorphonuclear leucocytes. Blood cultures, vaginal swabs, and culture of the Utus paste, from the same tube used, subsequently showed no culture, either aerobically or anaerobically. A lower nephron nephrosis developed, with her blood urea rising to 200 mg. on the ninth day after the injection of the paste. She eventually, however, recovered, with clinically normal pelvic organs.

Summary. A case of profound shock, enlarged liver and polymorphonuclear leucocytosis associated with renal damage following the use of intra-uterine paste. This case had many features of an anaerobic infection, but this was not proven bacteriologically.

The results in the 32 cases show that 9 cases had complete abortions subsequently. In 18 cases the foetus was passed but the placenta was retained, and in 5 cases this method was ineffective. In all those cases which aborted completely or incompletely the average length of time for the passage of the foetus was 2 days with a range of 1 to 4 days.

Discussion

The ingredients common to practically all intra-uterine pastes are soap and small quantities of iodine as potassium iodide, together with aromatic tinctures such as benzoin, myrrh or thymol. Leunbach (1931) published his formula for Provocol, also known as Leunbach's paste. Barns (1947) published the formula of the intra-uterine paste used at University College Hospital.

Up to 1932, there had been 25 fatalities reported in the literature following the use of intra-uterine paste. Engelmann (1932) reviewed the dangers of using "Interruptin" and noted 12 deaths due to fat embolism, and 5 deaths due to air embolism. Döderlein, in a letter to Riddell (1932), casts some doubt on the accuracy of the causes of death in many of the recorded cases due to the paucity of pathological and microscopic evidence taken at post-mortem. However, the Federal Minister of the Interior prohibited the use of Provocol in Germany, except by a physician's prescription, and on the physician's responsibility as to the outcome. The American Medical Association issued warnings against its use in Editorials in 1932 and 1938. Weilerstein (1944) classified the complications following the use of intra-uterine paste as seen in the United States, and gives as examples cases showing each type of effect. He lists its manifestations as follows:

1. Systemic effects.
   - A. Haemolysis, general and severe, resulting in death or mild, resulting in haemolytic jaundice.

B. Pulmonary embolism, sometimes fatal.
C. Generalized septicaemia, with fatal results, or with recovery, but with local residua.

2. Local effects.
A. Inflammation and its sequelae such as sterility due to tubal occlusion, peritonitis, and necrosis of uterine wall.
B. Bleeding as either severe acute haemorrhage, or prolonged continued bleeding

Many of the manifestations listed by Weilerstein may, of course, occur whichever method of therapeutic abortion is attempted. Acute haemorrhage, septicaemia, and pelvic infection may occur after the use of laminaria tents, dilatation of the cervix and piecemeal removal of the uterine contents or hysterotomy. Perforation of the uterus is a well-known hazard of any intra-uterine manipulation, and is especially likely to occur in the pregnant uterus. Tietze (1950), in a review of 3,600 therapeutic abortions, using various methods, in New York in the years 1943–1947 found 50 deaths, 7 of which were directly due to the operative procedure. Barns (1947) found that the morbidity in terms of pyrexia was no higher with intra-uterine paste than in cases aborted by other methods.

D'Amour and Kiven (1935) in animal experiments showed that in rats Leunbach's paste in standard concentration causes intra-uterine death and abortion, and in 6 out of 44 rats death within one month. Post-mortem findings in these latter cases showed multiple large pelvic abscesses. The findings in experiments with rats, as D'Amour and Kiven point out, cannot be accepted as proof that similar results would occur in humans, but it is of some significance that Weilerstein (1944) cites 3 cases of pelvic infection or peritonitis, with 1 death which at post-mortem showed a similar picture. Straus and De Nosaquo (1945) report a similar death from peritonitis, due to penetration of the uterus by the abortifacient paste.

Sterility as a sequel is also disputable. It is as likely to follow sepsis. Barns (1947) does not think it is a serious likelihood, although he has no evidence apart from the fact that 4 of his 71 cases subsequently conceived. No detailed follow-up was undertaken. It would be extremely difficult to prove what role intra-uterine paste plays in any subsequent tubal occlusion. A follow-up of this type of patient for later pregnancies would be inconclusive, as many of them are advised against a further pregnancy, due to the fear of a recurrence of the condition which was the indication for their previous therapeutic abortion. The fact that the paste reaches the tubes during the abortion was shown by Barns (1947). He added Neohydriol to the paste, and showed radiologically that in some cases the paste passed into the tubes, and 4 days after the abortion was still present in the peritoneal cavity. D'Amour and Kiven (1935) in experiments on rats showed that Leunbach's paste very definitely caused sterility in these animals.

Haemorrhage either as an acute or as a continuous loss was not seen in this series. The 2 cases readmitted for haemorrhage had retention of a piece of placenta. Barns (1947) gives 3 cases of continued bleeding, and 1 case of menorrhagia in his series of 71 cases, which he thought probably due to hyperaemia of the endometrium, caused by the chemical irritation of the paste. Weilerstein (1944) mentions 1 case of acute haemorrhage.

How often the paste enters the blood stream is difficult to say. It occurred twice in this series of 32 cases. Weilerstein (1944) cites 3 cases—2 of which died. Barns (1947) in 71 cases had no incidence. The speed of injection rather than the amount injected probably influences its incidence as, within limits, the faster the speed the greater the pressure used in injection. However, in the 2 cases where haemolysis occurred the speed of injection was 3 c.cm. per minute and the amount given was normal for the stage of pregnancy. In the case reported by Weilerstein (1944) where there was complete haemolysis, the amount given was 5 c.cm. The speed of injection was not stated. It is possible that the patient may complain of subjective symptoms which are masked by anaesthesia but which may give some warning that intravascular spread is taking place. If this is so then it is important that all cases should be dealt with without anaesthesia.

The percentage of successful abortions following this method varies. In this series, it was 27 per cent completely successful with a further 54 per cent aborting the foetus, but retaining the

placenta. Barns (1947) reports a success rate of 80 per cent. Weilerstein, from various sources, gives a success rate of 50 per cent. Otto, cited by the American Medical Association (1938), found evacuation complete in only 8 out of 24 cases. Leunbach had to curette only 12 out of 150 cases. It seems that the percentage of success depends to some extent on how long an interval elapses between the abortion of the foetus and the delivery of the placenta. In this series, the placenta was always removed if retained longer than 24 hours. Probably if left longer, and the patient given ecbolics, the complete success rate would be higher.

Summary

A review of 32 cases in which intra-uterine paste was used to induce therapeutic abortions has been made.

Two cases which exhibited severe complications have been reported.

An attempt has been made to review critically and re-emphasize the dangers inherent in the use of these pastes.

Our thanks are due to Dr. K. Mendl for his interpretation of the radiograms in Case A.

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TREATMENT OF ECLAMPSIA WITH BROMETHOL

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TRIBROMETHANOL or Bromethol has been used for a long time as a basal anaesthetic. But as a sedative and anticonvulsant it was first tried in the treatment of eclampsia by Conrad in 1927. Subsequently, Dewar and Morris (1947) used it in 44 cases of eclampsia from 1943 to 1947. Campbell and Burton (1952) claimed excellent results when they treated 36 cases of eclampsia with bromethol without a maternal death. In our hospital, we have been using this drug from January, 1951.

It is a powerful anticonvulsant and we are convinced that it is a better sedative than morphia. This observation has been made after a close study of cases treated with morphia, paraldehyde and chloral and bromide (rectally). Also in severe varieties of eclampsia, where morphia failed to control the recurrent fits, bromethol was found to check the convulsions effectively. The dose of bromethol is 0·1 ml. per kilo weight of the body. An average South Indian patient weighing about 100 pounds will need about 4·5 ml. of bromethol which is mixed with 5 ounces of water to form a solution of about 2·5 per cent and then administered per rectum as a retention enema. It takes about half an hour for the rectal drip to be completed. But in 10 to 15 minutes after the commencement of the drip the patient becomes quiet. The effect lasts for about 3 to 5 hours and if indicated it can be repeated not earlier than 3 hours after the first dose. The modified treatment now adopted in the Lying-in Hospital was started on 14th August, 1952 though bromethol was in use earlier, but the quantities used and the scheme were slightly different.

MATERIAL

From 14th August, 1952 to 31st December, 1953, 130 cases of eclampsia were admitted into the hospital. Of these 84 or 64·62 per cent were primigravidae and 46 were multiparous women.

TABLE I

The Age Group and Period of Pregnancy

Age Group	No. of Cases	Period of Pregnancy	No. of Cases
15 to 20 years ..	87	Up to 28 weeks ..	7
21 to 25 years ..	25	28 to 32 weeks ..	14
26 to 30 years ..	12	32 to 36 weeks ..	11
Over 31 years ..	6	36 weeks to full term	62
		Post-partum ..	36
	130		130

The eclampsia was ante-partum in 54 cases (72·3 per cent) whilst 36 patients (27·7 per cent) had convulsions after the delivery, most of them within a few hours following the confinement. Five patients had fits over 24 hours after the delivery and in 1 case the fits came on for the first time on the 5th day of the puerperium. Among the clinical signs, there was a surprisingly high incidence (45 per cent) of patients without any obvious oedema.

METHOD OF TREATMENT

On admission, the patient was given 4 ml. of bromethol in 5 ounces of distilled water per rectum by the drip method. Soon after sedation,

one pint of 20 per cent glucose was given by intravenous drip; and into the drip was added 10 ml. of 10 per cent calcium gluconate and 100 mg. of Vitamin C. Vitamin B Complex 2 ml. (containing 50 mg. of Vitamin B_1 per ml.) was given intramuscularly. Five hours following the first bromethol, whether there was a fit or not, the second bromethol was given rectally. Subsequent bromethol if necessary was administered 6 hours after the first bromethol. If the patient had a fit in spite of the sedation, the bag of membranes was artificially ruptured. On admission, if the foetal head was at the pelvic or vulval outlet, the patient was delivered with the forceps and then bromethol was given. One more pint of 20 per cent glucose was given intravenously after each operative delivery. The urine output was recorded in every case. As a prophylactic against aspiration pneumonia penicillin 200,000 units was given intramuscularly every 8 hours. No morphia or any other sedative was used in this series of cases. For the guidance of medical officers and the nursing staff these instructions were typed out and displayed in the Labour Ward.

Results

Mother: In 85 patients (65·5 per cent) there was no recurrence of fits after the first bromethol. In 112 patients (86·2 per cent) no convulsions were noticed following the second bromethol.

Table II

Number of Doses of Bromethol Used per Patient

Number of Times Bromethol was Used	No. of Patients
One dose of bromethol only	5
Two doses of bromethol	104
Three doses of bromethol	19
Four doses of bromethol	1
Six doses of bromethol	1
	130

It may be noticed that 2 doses of bromethol, each 4 ml., were sufficient in most (80 per cent) of our cases, though about 14·6 per cent had to be given bromethol thrice. In one case (No. 3362/53) the patient had 16 convulsions in the course of 24 hours and was treated with 2 doses of bromethol, 100 mg. pethidine hydrochloride and finally 0·5 g. Kemithal Sodium intravenously as fits could not be controlled with bromethol alone. Another patient (No. 3925/52) had 16 fits in the course of as many hours and could be controlled with 4 doses of bromethol given at intervals.

Out of 130 cases there were 7 deaths, a mortality rate of 5·4 per cent.

Effect on the Foetus

There is no evidence that bromethol produces depression of respiration either in the mother or in the foetus. Out of 130 cases, 1 ended in an abortion and 4 were not delivered in the hospital. The total number of babies was 125 and of these 14 were stillborn, giving a gross foetal mortality of 11·2 per cent. Ninety-one babies were born to the ante-partum and intra-partum group of cases and of these 78 were live born (86·9 per cent) and 13 stillborn, of which, in 8, the foetal heart was inaudible on admission. Bromethol was not considered responsible for any of the stillbirths. There were 16 neonatal deaths, 8 due to prematurity in the ante-partum and intra-partum group and 4 in the past-partum group of cases.

When we started the bromethol therapy in 1951, we were giving only one dose of bromethol as a routine. It was repeated only if there was a fit after the first bromethol. But the number of cases which required the second dose was large and, since the repetition of fits had a deleterious effect on the patient's general condition (the maternal mortality in a series of 64 cases up to August, 1952 was 12·5 per cent), the second bromethol was added with gratifying results as shown in this paper. In our series of cases no obvious liver damage was noticed. The kidney is the obligatory route of excretion of bromethol and deficient renal function and accumulation of drug with prolonged narcotic effect has been mentioned by Campbell and Burton (1952). The renal excretion is definitely helped by the hypertonic glucose. Campbell and Burton again have stated that with avertin there is a decrease in the blood and cerebrospinal fluid pressure which helps in its sedative action as an

TABLE III

Comparison of the Results of Bromethol Therapy with Those Obtained by Other Workers

	Dewar and Morris	Campbell and Burton	Lying-in Hospital, Madras
Total No. of Cases	44	36	130
Recurrence of fits after bromethol	7 per cent	25 per cent	34·6 per cent after first bromethol 13·8 per cent after second bromethol
Foetal Mortality	30·6 per cent	28·9 per cent	11·2 per cent
Maternal Mortality	4·5 per cent	Nil	5·4 per cent
Maximum dose	6 doses in 24 hours	—	6 doses in 78 hours

efficient anticonvulsant. The contra-indications for bromethol therapy are anuria and pulmonary oedema.

SUMMARY

Bromethol is a good sedative and anticonvulsant in the management of eclampsia.

A series of 130 cases of eclampsia were treated from 15th August, 1952 to 31st December, 1953. In about two-thirds of the patients, no fits were noticed following the administration of the first dose of bromethol per rectum. With the second doses 5 hours later in only 13·8 per cent did the convulsions recur.

The maternal mortality was 5·4 per cent and the gross foetal mortality 11·2 per cent.

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FOETAL RENAL HYPOPLASIA AND THE ORIGIN OF AMNIOTIC FLUID

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THE purpose of this paper is to discuss the role played by foetal urine in the formation of amniotic fluid. Two cases, one of bilateral foetal renal agenesis and one of severe renal hypoplasia, both of which were associated with a striking lack of amniotic fluid, will be reported to illustrate the discussion. It is also proposed to mention some of the characteristic features of renal agenesis.

THEORIES AS TO THE FORMATION OF AMNIOTIC FLUID

There are 4 current theories which were admirably reviewed by Shaw and Marriott (1949):

(1) *The fluid is a transudate from maternal vessels*

The evidence usually quoted is the appearance of hydramnios in decompensated maternal heart disease or liver disease in pregnancy.

(2) *The fluid is a transudate from the foetal circulation*

The association of hydramnios with chorioangioma, uniovular twins, and anencephaly, is given as evidence in favour of this view.

(3) *The fluid is a secretion by the amniotic epithelium*

As well as the histologically-proven fact that amniotic epithelium is secretory, the evidence classically quoted in support of this theory is that the injection of substances, chiefly organic dyes, into the maternal circulation leads to their appearance in the fluid, but not in the foetal tissues or urine. Shaw and Marriott, on the basis of such experiments, stated that there can be little doubt that the amniotic epithelium is the main source of the fluid. On the other hand, as Needham's (1931) review showed, there is experimental evidence which to a certain extent disproves the claim that substances of this type, when injected into the maternal circulation, do not appear in the foetal tissues or urine.

(4) *The fluid consists mainly of foetal urine*

As Needham pointed out, the anatomical connexion between the amniotic fluid and the foetal excretory apparatus is clearly evident. Moreover, the steady rise in the proportions of ammonia, urea, and uric acid in the fluid, demonstrated by Guthmann and May (1930), gives force to this statement.

Some experimental evidence in favour of the foetal urine theory is afforded by Wolff's (1904) work. He showed that double nephrectomy in pregnant animals was followed by hydramnios irrespective of the duration of pregnancy; since there were no other transudates in other parts of the body this was unlikely to be due to transudation from the maternal vessels which were overloaded with water unable to escape by its usual route. Also, he found that the greater was the number of embryos present the greater was the rise in the amount of fluid. However, as Wolff himself concluded, this was probably a compensatory phenomenon due to the loss of maternal excretory capacity, and was therefore not applicable to normal fluid formation.

The most important work indicating the part played by foetal urine appears to be that of Makepeace *et al.* (1931). They showed that foetal urine was hypotonic as early as the fourth month of pregnancy, at which time amniotic fluid was isotonic with maternal serum; at

term, however, the fluid became hypotonic. They therefore concluded that amniotic fluid originates as a dialysate in equilibrium with the maternal and foetal body fluids and that it becomes diluted by the hypotonic foetal urine as pregnancy progresses. In other words, amniotic fluid originates from both the amnion and the foetal kidneys, a conclusion which offers the most reasonable explanation of the normal processes of amniotic fluid formation.

Evidence Obtained from Cases of Renal Agenesis and Hypoplasia as to the Role of Foetal Urine

Bates, after discussing 14 cases of renal agenesis and hypoplasia associated with oligohydramnios or absent fluid, concluded, from these and a series of 24 cases studied by Bardram (1930), that renal agenesis was always associated with the absence of amniotic fluid, and that therefore there existed a direct relationship between the production of foetal urine and the volume of the fluid. Also, many authors have recorded cases of congenital obstruction to the lower urinary tract with the retention of urine above the obstruction. It is assumed from these that the kidneys have functioned and that foetal urine therefore forms part of the amniotic fluid (Bertkau, 1921; Schiller and Toll, 1927; Shaw and Marriott, 1949; Kinnunen, 1951).

Two cases are now to be reported which seem to support the conclusion reached by Bates (1933).

Case Reports

Case 1. Bilateral Renal Agenesis

Mrs. K.M.W., aged 37, primigravida, with a history of 8-years involuntary sterility, had a normal pregnancy until the 34th week, when a breech presentation was diagnosed. This could not be altered by version and, when she developed essential hypertension (140/100 mm.) at term, an elective Caesarean section was performed on the 9th December, 1953. Although she had had some desultory labour pains in the few hours preceding the section there was no evidence of ruptured membranes. At operation both the obstetrician and his assistant remarked on the complete absence of amniotic fluid. The infant, a male, weighing 6 pounds 6 ounces, was severely asphyxiated. It was noticed that the nose was very flattened, with increased distance between the eyes, and that the ears were particularly large and "floppy". There were no other external abnormalities. Breathing was not satisfactorily established, remaining very rapid and shallow from the onset. The child died 1 hour after birth. Nothing remarkable was noticed about the macroscopic appearances of the placenta and cord.

Post-mortem findings (Dr. A. C. Counsell). The infant was well formed except for the flattened nose and lack of chondrification of the ears. Although the thoracic cavity was normal, the lungs showed marked hypoplasia. The adrenals were normal in size, appearance, and position. Both kidneys were completely absent, the ureters ending blindly above in some tissue which proved to be adrenal tissue on section (see Fig. 1). The bladder was empty, both ureteric orifices being patent. Other organs, including the prostate, penis, and testicles, were normal in size and position. The seminal vesicles were not looked for. The placenta showed hyperaemia of the villi, and some haemorrhage had occurred into the cord; the membranes appeared normal and were not examined histologically.

Case 2. Bilateral renal hypoplasia

Mrs. N.L., aged 34, had a normal pregnancy until the 34th week when an oblique lie of the foetus, with the head towards the left iliac fossa, was diagnosed. This could not be altered. X-ray examination showed, in addition to the oblique lie and a normal pelvis, a hand and a foot presenting in the pelvic brim. This abnormal lie and presentation persisted until 10 days past the expected date of delivery, when an elective Caesarean section was performed on the 29th September, 1949. It was particularly noticeable that amniotic fluid was almost completely absent. The infant, a female weighing 6 pounds 11 ounces, was severely asphyxiated. Its head was of a peculiar shape and looked as though it had been moulded to the shape of the lower uterine segment. There were no other obvious external abnormalities. Respiration was not satisfactorily established and the infant died 3 hours after birth. The placenta was macroscopically normal but the cord was thin and looked unhealthy. The condition of the membranes was not noted.

Post-mortem findings (Dr. L. F. Brown). "The body was that of a recently born, mature female infant. The head was of curious shape with prominent frontal bones and pointed occiput. In addition one parietal bone was more flattened than the other. Both feet showed severe talipes equino-varus, presumably from pressure *in utero* because of the absence of liquor. This was probably the cause of the skull deformity. The lungs were almost completely devoid of aeration. The respiratory tract was clear.

"Both kidneys were completely fibrotic and were represented by small nodules of firm fibrous tissue about the size of a pea. Section of these showed a very few scattered glomeruli and tubules amongst fibrous tissue. The adrenals were normal. The bladder was empty; both ureters were present, ending in the small fibrous nodules mentioned. Uterus, tubes and ovaries were present. Both ovaries contained cysts. There was no evidence of other congenital anomalies."

The placenta, cord, and membranes were not sent for histological examination.

Comments on These 2 Cases and on Foetal Renal Agenesis and Hypoplasia in General

(a) *Frequency:* Bilateral renal agenesis is said to be rare. Up to and including Sylvester and Hughes's (1954) report, 175 cases have been described in the literature. Potter (1946) found an incidence of 0·4 per cent in 5,000 autopsies performed at the Chicago Lying-In Hospital during a period of 10 years. Sylvester and Hughes's 4 cases and Case 1 of the present series were all delivered at the West Middlesex Hospital, giving an incidence in this hospital of approximately 1 per 3,000 births. This seems to show the incidence is not so small as previously recorded.

Hinman (1940) and Nation (1944) insisted on the importance of distinguishing histologically between true agenesis and severe hypoplasia. Undoubtedly, as noted by Amolsch (1937), some cases of hypoplasia are included in the totals of agenesis in the literature; consequently the true numbers or incidence of agenesis or hypoplasia cannot be accurately stated.

(b) *Sex-linkage:* Renal agenesis shows a more striking tendency towards sex-linkage than any other congenital malformation except anencephaly; it is approximately 3 times more common in males than in females (Amolsch). This may be connected with the increased importance of the Wolffian duct system in the male. The ureter develops as an outgrowth from the Wolffian duct and the development of the metanephrogenic cap may fail in the absence of the ureter (Rainer, 1931). Nation (1944) agreeing with this view, stated that the ureters were nearly always absent—this is not supported by the 2 cases reported here, as in each case the ureters were fully developed. In view of the sex-linkage displayed by renal agenesis it is worthy of note, as Potter pointed out, that it has never been recorded with anencephaly, a condition predominantly associated with female foetuses and, incidentally, hydramnios.

(c) *Other abnormalities:* Renal agenesis is usually associated with malformations of other organs. Most often the derivatives of the Wolffian ducts (in the male) and the Müllerian ducts (in the female) are affected. Amolsch (1937) stated that Fallopian tubes were usually present but that the uterus and vagina were absent. The female child here reported had normal genitalia (except for the ovarian cysts); this is probably because the condition was a severe renal hypoplasia and not a true agenesis.

(d) *Diagnosis:* Some points which may aid in the diagnosis of the condition ante-mortem are well illustrated in Case 1: (i) *The characteristic facies*—this was stressed by Potter and comprises large epicanthic folds, increased distance between the eyes, large poorly-chondrified ears, and a general appearance of premature senility. (ii) *Severe respiratory distress*—this undoubtedly is caused in many cases by the pulmonary hypoplasia found in such infants.

Discussion

Bates (1933) has pointed out that cases of renal agenesis and hypoplasia associated with oligohydramnios are of great importance when one considers the question of the source of amniotic fluid, for proponents of the foetal urine theory look for their greatest support in those instances of oligohydramnios associated with foetal urinary anomalies. As previously mentioned, it seems probable from the work of Makepeace *et al.* (1931) that the amniotic fluid is both maternal and foetal in origin. If this and the importance of renal hypoplasia as regards the foetal contribution be conceded, why is it that some cases of renal agenesis and severe hypoplasia, as illustrated by Bates's and the present writer's cases, are associated with complete or almost complete lack of amniotic fluid? One would expect a certain amount of fluid formed by the amniotic epithelium to be present. The explanation may lie in a co-existent abnormality of the amnion such as a diffuse inflammatory change as was described by Schiller and Toll (1927) and which they believed destroyed the secretory function of the epithelium.

A much more probable explanation, however, and one which supports the importance of the foetal urine is to be found in Landing's (1950) paper on amnion nodosum. This is a condition where small nodular masses are found on or in the amnion or occasionally projecting into the cleft between the amnion and chorion. The amniotic epithelium is absent or exists only beneath these masses as strips or inclusion cysts.

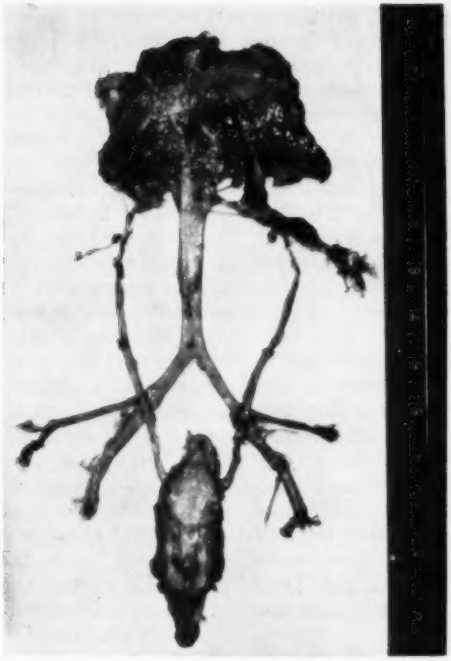

FIG. 1

Dissection of Case 1 showing bladder (ureteric orifices marked by bristles), ureters, abdominal aorta and its main terminal branches, and part of the diaphragm. The adrenals have been removed. Sections of the tissue at the upper end of both ureters showed adrenal tissue only.

The appearance of these nodules, according to Landing, suggests that they result from the adhesion of masses of amniotic squames to the amnion with subsequent degeneration of the epithelium and its invasion by connective tissue. Of Landing's 8 cases of this condition, the 5 infants who were subjected to autopsy showed major abnormalities of the urinary system, including 2 with renal agenesis. The majority of cases of amnion nodosum are apparently associated with oligohydramnios and the author suggested that the amniotic squames in abnormally concentrated fluid (which in the 2 cases of renal agenesis at least could not contain foetal urine) adhere to the amnion and cause degeneration of the epithelium. This would lead to the loss of that part of the amniotic fluid produced by the epithelium. Although the co-existence of amnion nodosum would have explained the absence of fluid in the reported cases, it is to be regretted that it was not known of and therefore not looked for at the time of delivery.

Even if the absence of fluid be thus explained there still remain those cases of renal agenesis where the fluid is normal in amount—as in one of Sylvester and Hughes's 4 cases—which call for an explanation. Browne (1950) stated that the fluid in renal agenesis is usually normal in volume and may indeed amount to hydramnios. In none of the recorded cases, however, is hydramnios an associated feature (Needham stated that Hochsinger recorded 1 such case in 1899, but, according to Bates, this one was associated with absence of amniotic fluid). Moreover, cases where the fluid is normal are very much in the minority, and usually (Potter's 20 cases, Nation's 4 cases, 3 of Amolsch's 4 cases) there is no mention of the amount. As Potter surmised from this lack of mention of fluid, it is probably taken for granted that the fluid has escaped prior to hospital admission.

Another explanation of the presence or apparent presence of normal amounts of fluid in some cases of renal agenesis is found in the current concept of the circulation of the amniotic fluid. This is being continuously produced and continuously reabsorbed, the latter process taking place via the foetal alimentary and respiratory tracts. Normally production and absorption are in balance—Vosburgh *et al.* (1948) showed that the water of the fluid was replaced every 2·9 hours. Anencephalic foetuses, which are unable to swallow, and foetuses with duodenal atresia (Mengert and Bourland, 1945), are associated with hydramnios owing to absorption failing to keep pace with production. Possibly oesophageal or duodenal atresia (the association of pyloric stenosis with male infants and of male infants with renal agenesis is to be noted here) or pulmonary hypoplasia, may have been overlooked in autopsy examinations performed on such infants. In only one case of renal agenesis in the literature is duodenal atresia mentioned as a concomitant abnormality—this was one of Potter's cases where the amount of fluid was not mentioned. Potter also noted in 1946 that she was the first to describe pulmonary hypoplasia in association with renal agenesis.

Conclusions

The evidence seems to show that amniotic fluid is derived both from the amniotic secretion and from foetal urine. In addition, it appears probable that foetal urine plays a more important part than has hitherto been generally acknowledged. Cases of renal agenesis and hypoplasia associated with oligohydramnios are of some account in maintaining this view. It seems possible to amend Bates's statement that renal agenesis "is apparently always associated with an absence of amniotic fluid" to ". . . nearly always . . ." and to explain the absence of the amniotic epithelium component of the fluid on the basis of Schiller and Toll's diffuse inflammation of the membranes, or Landing's condition of amnion nodosum. It is not unlikely that these two authors are describing the same condition. Finally, cases of renal agenesis and severe hypoplasia with normal amounts of fluid are very much in the minority compared with cases associated with oligohydramnios; they do not negative the importance attached to foetal urine in the formation of amniotic fluid, the presence of which may possibly be explained by a mechanism of reduced absorption, to be found on a more careful search for associated upper intestinal tract atresia or pulmonary hypoplasia. What would have been a case of hydramnios with an otherwise normal infant becomes a case

with a normal amount of fluid in an infant suffering from renal agenesis or severe hypoplasia.

In recording future cases of bilateral renal agenesis and hypoplasia, therefore, it is suggested that a careful note be made of three observations.

(i) the amount of amniotic fluid present,
(ii) the macroscopic and microscopic appearances of the placenta and membranes,
(iii) the presence or absence of pulmonary hypoplasia and atresia of the upper part of the intestinal tract.

In order to recognize such foetuses it is important to be familiar with the facies described so well by Potter, so that the amount of fluid may be checked immediately and the placenta and membranes saved for a detailed examination later.

Summary

(1) Amniotic fluid is probably normally derived from the amniotic epithelium and foetal urine, with transudation from maternal and foetal vessels possibly playing a part in pathological conditions.

(2) It appears from a consideration of cases of oligohydramnios associated with major foetal urinary anomalies that foetal urine plays a more important part than has been previously conceded. A case of bilateral renal agenesis and one of severe renal hypoplasia, both associated with lack of amniotic fluid, are presented in support of this contention.

(3) The combination of severe foetal respiratory distress and lack of amniotic fluid, together with the appearance of premature senility and large "floppy" ears in the infant, should suggest the diagnosis of renal agenesis in a newborn infant.

(4) The absence of the contribution of the amniotic epithelium to the fluid in some cases of renal agenesis or severe hypoplasia, and the presence of normal amounts of fluid in others, is explained.

Acknowledgments

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DYSTOCIA CAUSED BY CONGENITAL HYDRONEPHROSIS AND BLADDER DISTENSION

BY

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CONGENITAL hydronephrosis is a not uncommon condition. Most cases are discovered after the neonatal period, in infancy and childhood, and few are severe enough to be a cause of stillbirth. The most common single factor is some valvular obstruction in the urethra (Young and McKay, 1929).

Only 2 cases have been reported where no mechanical obstruction in the urethra could be found, and where the distension was such that the abdomen and bladder had to be perforated before delivery was possible (Edgecombe, 1930; Savage, 1935). Edgecombe believed that the aetiology in her case had been a neuro-muscular imbalance, due to defective innervation of the bladder, and the same aetiology was implied by Savage. No evidence supporting this could be given except the absence of any other apparent cause.

CASE REPORT

The mother was admitted to hospital in August, 1954, because of oedema and albuminuria. She was in the seventh month of her sixth pregnancy. All the previous children had been normal full-time deliveries with no congenital deformities and all were alive and well. Investigations revealed a moderate albuminuria (50 mg. per 100 ml.), slight ankle oedema and a haemoglobin of 7·4 g. (50 per cent. of normal). This was treated with a transfusion of 3 pints of packed cells after which her haemoglobin rose to 80 per cent of normal. Her Wassermann reaction was negative. The foetus was a vertex presentation, and was at this date firmly engaged.

Two weeks after admission she went into labour. This progressed normally at first and the head and shoulders were delivered without much difficulty. Then no further progress could be made. It became evident, when she was examined under anaesthesia, that the dystocia was due to the enormously distended abdomen of the foetus. Eventually this had to be perforated and the delivery completed after the release of some 30 ounces of pale yellow fluid. A brisk post-partum haemorrhage occurred which required further blood transfusion.

The Infant. The infant was a male weighing 4 pounds 8 ounces. The anterior abdominal wall had been ruptured from just above the symphysis pubis to 3 centimetres above the umbilicus. The skin of the abdomen was wrinkled and lax, some separation of the recti had occurred and the lower ribs were splayed outwards. A bilateral talipes equino-varus was present. There were no other external abnormalities.

On further examination it was obvious that the fluid released at delivery had come from a greatly distended bladder. This organ had been perforated 4 centimetres over the bladder neck and was now empty, but at full capacity it had filled the greater part of the abdominal cavity raising the level of both domes of the diaphragm. The bowel had been crushed against the posterior abdominal wall and was empty.

The bladder wall was smooth and showed many spider-shaped haemorrhages on the inner surface; the average thickness of the wall was 1·5 millimetres. There was no evidence of trabeculation. Bilateral hydro-ureters, each 3 centimetres in length, and a gross bilateral hydronephrosis were present. Only a thin rim of kidney tissue 3 millimetres thick remained. The remaining organs showed no specific changes and there were no other congenital abnormalities.

The urethra was gently probed from both the bladder and the external meatus, and was found to be patent. It was laid open throughout its whole length but no valvular or other obstruction could be demonstrated.

Histology. Sections from the bladder neck and selected areas of the urethra were studied. No hyperplasia or hypertrophy in the region of the bladder neck as described by Vail and Stone

(1947) was seen and no abnormality in the urethra could be demonstrated. Because of the close association between dilatation of the bladder and agenesis of the abdominal muscles (Obrinsky, 1949) blocks taken from the anterior abdominal wall were sectioned but, apart from evidence of stretching and thinning of the muscles concerned, no abnormalities were seen.

Discussion

The infants in the cases previously reported had other abnormalities, both had bilateral talipes equino-varus, and one, Edgecombe's case, had an imperforate anus. It is evident that in each there was a minor degree of urethral obstruction, a phimosis in Edgecombe's case, and a partial stenosis of the penile urethra in the case reported by Savage. Neither of these was considered to be severe enough to cause gross bladder distension and hydronephrosis.

There was no obstruction demonstrable in the present case, and histology of well-known sites of obstruction showed no abnormality. It seems likely, therefore, that this case is comparable with the two previous cases as reported, and that the hydronephrosis was due to a neuro-muscular imbalance in the region of the bladder neck. The occurrence in all three of a bilateral talipes equino-varus is interesting.

Comparing the relative distension of the bladders, and the duration of the pregnancies in these three cases, it is evident that all three had a capacity of about one litre, and the time of onset of the distension was approximately the same. The normal capacity of the urinary bladder at birth is between 40 and 70 millilitres.

It has been suggested by Caulk (1923) and Bell (1946) that a similar congenital neuro-muscular imbalance can occur at the distal ends of both ureters causing hydronephrosis without bladder distension, and, since in this situation valvular or other obstructing mechanisms are less likely to be missed, the hypothesis has a firm basis. These lesions because of their site rarely give rise to abdominal distension great enough to cause serious difficulty during labour.

It seems likely, therefore, that a neuro-muscular imbalance possibly due to defective innervation can occur at various points in the urinary tract. Some of these in the region of the bladder neck can be severe enough to cause gross bladder distension requiring perforation at delivery. There is an obvious similarity in this with congenital megacolon (Hirschsprung's disease) but the conditions have not been observed together.

Summary

(1) A case of congenital hydronephrosis and gross bladder distension causing dystocia is reported.

(2) The case is unusual in that no mechanical urethral obstruction could be found.

(3) It is suggested that the conditions was caused by a neuro-muscular imblance.

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FIG. 1

VAGINAL PLUG FOR PROCIDENTIA IN ELDERLY WOMEN

BY

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FOR some years past I have been attempting to devise a comfortable vaginal plug to act as a support to the womb in elderly women suffering from procidentia, who cannot retain a pessary, and who are too old or ill for operation. I have now succeeded, and have already 7 very grateful patients who say they can walk long distances and are free of dragging pains and frequency of micturition when using this vaginal plug.

The plug is like a test tube and is inserted on rising and removed on going to bed. It is made of clear perspex, is unbreakable, easy to clean and does not perish. The belt and tapes are similar to those of the Napier Cup and Stem pessary; they are worn outside the undervest for comfort. When an old lady has a sensible daughter who can use a needle and thread, I advise transferring the tape attachments to a boy's serpent buckle belt as this makes its fitting-on and taking-off a matter of seconds only. It takes some time for the patient to get used to the appliance which should at first be used for only a few hours daily (Fig. 1).

I find it is a great help in all cases to prescribe 1 mixed gland tablet daily from Mondays to Fridays—e.g., a Mepilin (B.D.H.), Hormostergon (Polypharma), Myxogen (Organon), Menopaxforte (Clinical Products), or Fermandren tablet (Ciba). A course of one of these tablets daily will cause the vaginal walls to become less degenerate, tender and thin, and emotionally the patient feels happier.

The ages of these 7 patients are 89, 81, 80, 73, 72, 55 and 40. The patient aged 40 is wearing a plug as a temporary measure whilst awaiting operation. The 55-year-old patient has been under treatment for cancer of the breast for some months and will be operated on later, if all goes well. The 72-year-old patient first reported to me with an impacted Napier Cup and Stem pessary, causing a vesico-vaginal fistula. I removed the stem from the injured bladder wall and 6 weeks later repaired the fistula. She is now happy with a vaginal plug. In another case, aged 73, the procidentia was so wide and large that the plug kept turning right around and coming out. An especially large plug was made—almost jam-pot size—and is a complete success.

The older the patient with procidentia, the greater seems the success. All those aged 89, 81, 80, 73 and 72, are especially grateful for the benefits derived from its use.

The plug can be cleaned by dipping it in boiling water; glycerine can be used as a lubricant, but is seldom necessary. The rubber attachments and the rubber stem immediately below the tube tend to perish, and require replacement at yearly intervals. The perspex tube is, unlike rubber, non-irritating so douching is seldom required. There is no danger of impaction or fistula as is the case with the Napier Cup and Stem pessary, and even ulcerated cervices improve and can heal whilst using this plug.

The older the patient and the greater the prolapse, the more helpful is the plug and the deeper the gratitude of the patient.

This apparatus is not always successful in apparently suitable cases, but these number less than 1 in 4.

The vaginal plug can be supplied by Messrs. Allen and Hanbury, Ltd., Wigmore Street, London, W.1.

FRACTURE OF THE SPINE IN PREGNANCY

BY

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FRACTURE of the spine in pregnancy is rare and will usually be found at times when civilian injuries are high, namely during aerial bombardment in wartime.

Nevertheless, perusal of the literature shows that very few cases have been reported. In 1932 Naujoks reported 3 cases of severe trauma in pregnancy, the injuries being sustained as a result of falls or road accidents. In one case, there was a fracture of the tibia and fibula; in the 2 others the injury was of the vertebral column and both occurred between the twelfth and sixteenth week of pregnancy.

In one of the cases, following a fall from a cart, there was transient loss of consciousness and, on recovery, the patient complained of severe pain in the back and inability to stand or walk. X-ray examination in this case revealed compression fractures of the bodies of the 6th and 11th thoracic vertebrae with a lesser degree of damage to the body of the 9th thoracic vertebra. The patient was treated by flat bed rest and her recovery was uneventful, she being delivered spontaneously at term, though no mention is made as to any modification in the method of delivery. The other case described by this author sustained injury after a road accident, the patient being found to have a compression fracture of the 9th thoracic veterbral body, there being, in addition, motor paralysis of both legs and paralysis of the bladder, the latter necessitating frequent catheterization. Although the pregnancy had not been disturbed, it was not found possible to lay the patient on her abdomen and it was thought wise to terminate pregnancy in this case. This was done abdominally, as it was felt that the adoption of the lithotomy position would worsen the spinal condition. After the termination, the patient was treated by rest, lying on her abdomen, and recovery was uneventful, the paralyses clearing completely.

The only other case of fracture of the spine in pregnancy which can be found is one recorded by Kolonja (1952). This occurred during an attack of tetanus at the 24th week of pregnancy and the bodies of the 3rd, 4th, 6th and 8th thoracic vertebrae were fractured. The case was treated with flat bed rest and the fractures healed, the patient being delivered at the 36th week of a living female infant, weighing 7 pounds.

All the cases mentioned above dealt with fractures at an early stage of pregnancy and little mention is made of the possible danger of delivery in such cases by the normal maternal attitude in the second stage of labour. The case record presented below is of a fracture occurring at a later stage of pregnancy and the method of treatment and the method of delivery are discussed.

CASE REPORT

Mrs. M.B., aged 31 years, attended the antenatal clinic for the first time on 1st January, 1954. Her last menstrual period had commenced on 10th September, 1953 and her estimated date of delivery was 17th June, 1954.

There had been no serious illnesses in the past, although the patient stated that her husband had pulmonary tuberculosis, which was now quiescent.

She stated that she had been well since the beginning of pregnancy and physical examination revealed no abnormality. The fundal height corresponded to a pregnancy of 16-weeks duration. Blood was taken for routine examination and X-ray of the chest carried out.

Blood. Blood group "A": Rhesus positive. Wassermann and Cardiolipin negative.

Chest X-ray. No abnormality was detected.

The patient subsequently attended at monthly intervals and no abnormality was found at these visits.

FIG. 1
X-ray of the lumbar vertebrae after the accident, showing the crush fracture to the 1st lumbar vertebra.

FIG. 2
Lateral X-ray of the lumbar vertebrae after the accident, showing the crush fracture sustained by the 1st lumbar vertebra.

FIG. 3

X-ray of the 1st lumbar vertebra after 7 weeks bed rest, showing a little calcification only taking place.

Admission to hospital, 10th April, 1954

The patient was admitted to hospital with a history that, whilst walking along the pavement, a hoarding had fallen and struck her on the side of the head, knocking her on to her side. She complained of a dull aching pain in her back dating from this time.

Examination on admission showed her general condition to be good, there being no complaints apart from the dull aching pain in her back. No obvious deformity of the back was detected and no localized tenderness was found. Examination of the central nervous system showed no abnormality. The fundal height was equivalent to a 28-weeks pregnancy and the foetal heart was heard.

X-ray examination of the spine was carried out, which revealed a crush fracture of the body of the first lumbar vertebra, with little displacement.

She was transferred to the fracture ward and was placed at flat bed rest. Whilst at rest in this position, the back pain subsided and, from the second day onwards, she was almost free of the pain. Flat bed rest was continued from the time of admission for a period of 7 weeks. She was then transferred to the antenatal ward, X-ray examination at this time showing little calcification only of the body of the first lumbar vertebra. The pregnancy had now reached the 36th week and the foetus was in the longitudinal position, the vertex presenting in the right occipito-anterior position. The head was not engaged, but pushed into the pelvis.

In view of the further X-ray report, the patient was seen in conjunction with the orthopaedic surgeon and it was thought wisest to spare the patient any movement which might lead to further flexion of the spine and that this could be effected best by delivering her at the time of full dilatation of the cervix with the obstetric forceps. She remained in the antenatal ward until 30th May, 1954, when she went spontaneously into labour, examination at this time showing the foetal head to be engaged in the pelvis.

The first stage of labour proceeded uneventfully, the patient being transferred to the labour ward on a stretcher every care being taken to avoid flexion of the spine. At the time of full dilatation of the cervix she was given atropine sulphate, 1/100 gr., intravenously and anaesthetized with nitrous oxide, oxygen, trilene and ether. Forceps delivery was carried out, the legs being held out straight by assistants, it being felt that flexion at the hips and knees was inadvisable. An easy forceps delivery of a living female infant, weighing 6 pounds, was carried out through a "J"-shaped episiotomy. The latter was repaired with interrupted vaginal catgut sutures and external nylon sutures after delivery of the placenta and membranes.

The puerperium was uneventful, the patient being kept at flat bed rest for the 3 weeks following delivery. Breast feeding had to be abandoned on account of poor lactation and the infant was given Bacille Calmette-Guérin (B.C.G. vaccine) 5 days after birth in view of the history of tuberculosis in the father. Seven days after delivery, the patient was measured for a surgical corset and she was allowed out of bed for the first time 3 weeks after delivery, wearing the corset. X-ray examination at this time showed consolidation occurring in the body of the first lumbar vertebra. She was finally allowed home 5 weeks after delivery, wearing the surgical corset.

Follow-up at the postnatal clinic and at the fracture clinic have shown the patient well, although she has some residual dull aching in the back.

Discussion

Fractures of the dorsi-lumbar vertebrae are usually sustained at the junction of the mobile and relatively immobile segments of the spine, the most commonly affected being the 12th thoracic and 1st lumbar vertebrae. Most of such fractures are sustained with the spine in an attitude of flexion, extension fractures being rare. The types of fracture which may be found in the former instance depend on the type of injury. Those in which the patient falls from a height in the sitting or standing position, or where a weight falls from above onto the patient, occur at a time when the spine is in an attitude of slight flexion and result in compression of one or more vertebral bodies. If the patient is stooping and a weight falls on the shoulders, the spine is sharply angulated into acute flexion and a comminuted fracture of the vertebra results. Finally, where the patient is struck from behind, there is a traversing momentum in addition to the flexion strain, a fracture-dislocation resulting. The commonest injury is the first described and usually involves more than one vertebral body. It should be remembered that there is usually no associated damage to the inter-vertebral disc, but that there is often strain to the inter-articular ligaments (Watson-Jones, 1943).

Diagnosis of injuries of the vertebral body of the types described is both clinical, where examination shows a prominence of the spinous process, and radiological, this latter being essential in all suspected cases of vertebral injury, for the patient may not complain of local tenderness in the back. Treatment usually consists of the application of a plaster jacket with the spine in the hyperextended position, such plaster extending from the pubes and groins to the clavicles anteriorly and from the gluteal cleft to the scapulae posteriorly. Subsequently, the patient should be encouraged to pursue normal activities and X-ray examination carried out at intervals to ensure that healing is taking place.

It is thought wise to leave the plaster in place for some 4 months before finally removing it.

In the described case, it was felt that the injury did not require such treatment. There is nowadays a tendency to treat crush injuries of the vertebral bodies, where there is little displacement, by rest in bed in the manner described and not to apply a plaster jacket. A further deterrent in the described case was the fact that the abdomen was enlarged by a progressive pregnancy and it is known that the cutting of a large window in a plaster jacket makes its efficiency doubtful.

Delivery was carried out in the manner described, all efforts being made to prevent further flexion strain on the spine. The adoption of the lithotomy position in the second stage of labour, either on the part of the mother or during forceps delivery, was thought to be particularly undesirable and was avoided in the way already described.

One further point is worthy of mention. The authors quoted earlier considered that pregnancy exerted a beneficial effect on the rate of calcification of the injured bones, but this observation does not appear to be borne out by the radiological evidence in the case described, for the lack of calcification, despite treatment, was one of the main factors which determined the method of delivery.

Summary

A case of fracture of the 1st lumbar vertebral body at the 28th week of pregnancy is recorded. Delivery was effected by forceps and the reasons for such delivery have been mentioned. The literature dealing with injuries to the vertebral column in pregnancy has been reviewed.

Acknowledgments

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A CASE OF SPONDYLOLISTHESIS IN PREGNANCY

BY

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SPONDYLOLISTHESIS is a very rare cause of obstetric difficulty. Snow (1954) found no case of spondylolisthesis in a series of radiological studies of over 16,000 pregnancies in New York City. The first case to be presented to the Edinburgh Obstetrical Society was by Johnstone and Thompson (1934–5). On investigation of the literature 65 cases were found, and only 18 of these have been reported in the last 40 years.

CASE REPORT

A 27-year-old primigravida attended the antenatal clinic with a history of having sustained a spinal injury in a diving accident when she was aged 13. This was treated by a bone graft to the lower lumbar and sacral vertebrae when she was 21 years old. She was 5 feet in height, and she limped a little because of slight shortening of her right leg. She had an unusually upright posture, due to exaggerated lumbar lordosis. An area of anaesthesia was found over the posterior aspect of the right thigh and buttock.

Pelvic examination failed to reveal any abnormality. The subpubic angle was approximately 90 degrees, the transverse diameter of the outlet was 9 to 10 cm., and the sacral promontory could not be reached. Radiological examination showed the typical forward dislocation of the body of the last lumbar vertebra relative to the first sacral segment. Pelvimetry showed that the obstetric conjugate measured 9·5 cm. (Fig. 1). The intertuberous diameter measured 8·9 cm., and the antero-posterior diameter of the outlet measured 10·4 cm. The subpubic angle was 90°.

In late pregnancy the vertex always presented, but the head never fixed in the pelvic brim. In spite of this, there was no definite clinical evidence of disproportion, and, in view of the radiological measurement of the conjugate of 9·5 cm., it was decided to conduct a trial of labour.

The patient was admitted 4 days before the expected date to allow close supervision of the early stage of labour. Seven days later she complained of backache, and this was soon followed by spontaneous rupture of the membranes, at 10 a.m. The foetal head was well flexed but not engaged, and on vaginal examination the cervix admitted one finger. At 2.30 p.m. short uterine contractions were occurring at intervals of 8 minutes but the head was still mobile. By 3.15 p.m. stronger contractions had pushed the head into but not through the brim, and a lateral X-ray showed the head above the brim in the right occipito-lateral position. Two hours later, after a good sleep, the patient wakened with strong 4-minute contractions. The head was now engaged, and the cervix was found to be three-quarters dilated. By 7.15 p.m. the cervix was fully dilated, and the head had rotated into the occipito-anterior position. Half an hour later episiotomy was performed and low forceps delivery completed because of foetal distress. It was also considered undesirable to submit the ankylosed vertebrae to any undue strain, such as might have occurred with strong bearing down efforts in the second stage of labour.

The child weighed 6 pounds 8 ounces (2·9 Kg.). The head was well moulded with reduction in the occipito-bregmatic diameter, which measured 8·9 cm.

Persistent low backache occurred in the puerperium, but was relieved by active exercises, supervised by the physiotherapist.

DISCUSSION

Aetiology

Spondylolisthesis is usually the result of traumatic fracture-dislocation of the laminae of the fifth lumbar and first sacral vertebrae. It is occasionally due to a congenital defect. Brailsford (1944) says that it is improbable that it is initiated by pregnancy, though Meyerding (1934) suggests that pregnancy will aggravate an established lesion.

Diagnosis

Careful antenatal care should disclose the deformity before labour. A history of injury to the back should be investigated, and a short leg, lumbar lordosis, or a short trunk with a pendulous abdomen may be found. Neurological signs are not usually evident (Meyerding, 1934) but aching in the legs or an area of anaesthesia may occur, as in the present case. Failure of the head

to engage at term in a primigravida, or a malpresentation, will direct attention to the possibility of an abnormality of the pelvic inlet. The diagnosis is finally established by a lateral X-ray of the lumbo-sacral vertebrae.

Management

Among 18 cases described in the last 40 years 8 cases were delivered by Caesarean section and 10 vaginally. In only 5 of the cases delivered vaginally were measurements of the obstetric conjugate available, and in each instance the measurement was more than 10 cm. Brews (1954) described a case in which the conjugate was reduced to 9·1 cm., and this patient was delivered by Caesarean section. When the conjugate is 9·5 cm., as in the present case, trial labour is suitable, and it is felt that trial of labour should be given a greater place in the management of these cases, especially if the deformity has received adequate orthopaedic treatment, which will prevent secondary narrowing of the pelvic outlet due to tilting forward of the sacrum. Assistance with forceps in the second stage is strongly advocated, both to relieve any further strain on the lesion and sometimes because of minor degrees of outlet contraction.

Prognosis for subsequent pregnancies

In all subsequent pregnancies the pelvis must be reassessed, as the lumbar lordosis may have progressed after delivery, with further forward tilting of the sacrum, thereby producing convergence of the lateral bore of the pelvis with narrowing of the antero-posterior diameter of the outlet. This same mechanism has a tendency to diminish the inclination of the plane of the pelvic brim with its angle to the horizontal. In this way an abnormal presentation would be more likely because of difficulty in engagement of the head, especially if the abdomen is more pendulous. If all the measurements are again satisfactory successful vaginal delivery may be expected. An unstable lie would be treated on its merits. Because a second or third baby is often larger than the first, Caesarean section may be necessary for this added reason alone.

Summary

(1) A case of spondylolisthesis in a primigravida is described. An assisted vaginal delivery following a trial of labour ensued.

(2) The diagnosis of the deformity is discussed, particularly when it is associated with pregnancy. Some suggestions as to the mode of delivery are presented.

The management of pregnancy and labour of the case presented was conducted at Pembury Hospital, Kent. I wish to thank Mr. E. D. Y. Grasby and Mr. I. E. J. Thomas for permission to publish the case, also Dr. T. S. Leedham for the radiological pelvimetry. I also wish to thank Mr. R. C. Percival for his comments.

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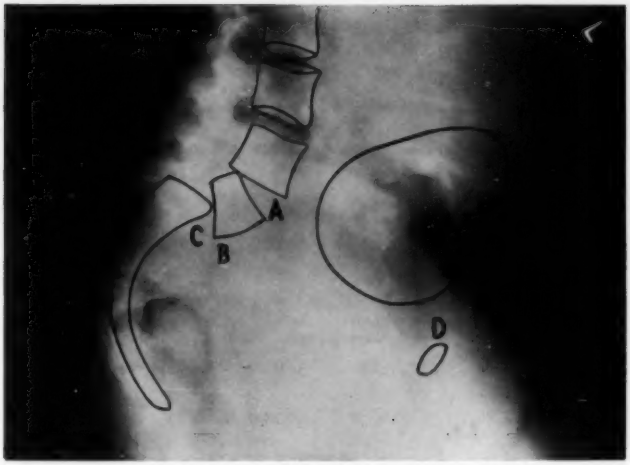

FIG. 1

Lateral radiological pelvimetry and explanatory diagram.

A—D 9·5 cm.—The obstetric conjugate.
B—D 10·8 cm.
C—D 12·1 cm.

A = Anterior superior border of lumbar 5 vertebra.
B = Anterior inferior border of lumbar 5 vertebra.
C = Anterior superior border of sacral 1 vertebra.
D = Posterior superior border of symphysis pubis.

FIG. 2

The subpubic angle = 90°.

MONO-AMNIOTIC MULTIPLE PREGNANCY

A Report of Five New Cases

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UNIOVULAR twins normally have separate amniotic sacs but they occasionally share a single one. In the latter case, the twins may be separate or conjoined. This has long been recognized but it has only been explained during recent years and that mainly by workers at the Carnegie Institution of Washington, who showed that the type of uniovular twinning varies according to the time at which the fertilized ovum divides (Hertig and Rock, 1945; Coulton, Hertig and Long, 1947).

The occurrence of mono-amniotic twins is generally regarded as rare but its incidence is as yet unknown and many cases probably pass unnoticed. It is commoner in the Fallopian tube than in the uterus. Arey (1923a) found 8 definite and 2 other possible cases in 36 unilateral tubal twin pregnancies which were the subject of his review.

During the period October, 1952 to June, 1954 there were delivered in Mill Road Maternity Hospital 99 sets of twins and 2 sets of triplets; amongst these were 5 cases in which 2 separate babies shared a common amniotic sac. This may not represent the true incidence of a mono-amniotic arrangement among multiple pregnancies because, during the preceding 5 years, there had been a further 259 cases of multiple pregnancy and mono-amniotic twinning was not recorded in any. Of the 5 cases personally encountered, only 4 can be regarded as genuine samples of mono-amniotic twinning. In the fifth there was a suggestion of a dividing membrane and it may be that there had originally been 2 compartments, the intervening wall having broken down later.

CASE HISTORIES

Case No. 1 (8257). Age 29 years

This patient had had 2 previous normal pregnancies ending in the spontaneous birth of healthy single infants at term. There was no history of multiple pregnancy in her family, but there were no less than 5 sets of twins among her husband's near relatives. In the pregnancy in question, twins were diagnosed at the 24th week and the only complication was moderate generalized oedema which developed at the 38th week, and which responded well to treatment by rest in hospital. Labour commenced spontaneously at the 39th week and the cervix was fully dilated after only 2 hours. Abdominal and vaginal examinations showed that both foetuses were presenting by the head. The membranes in front of the first head were ruptured artificially and this resulted in a profuse flow of liquor heavily stained with meconium. However, the foetal heart sounds remained normal and the leading head advanced rapidly to be delivered spontaneously with the aid of an episiotomy. The infant was slightly asphyxiated but soon revived. Vaginal examination was then made by the house surgeon who had delivered the first baby and he failed to find a second bag of membranes. It was thought that this must have ruptured unnoticed at an earlier stage, though no liquor had been seen to escape except at the time when the membranes were ruptured artificially. It was decided to proceed at once to forceps delivery of the second baby whose head had already entered the pelvic cavity. This operation was completed easily and quickly under analgesia provided by the trilene inhaler and an intravenous injection of 100 mg. of pethidine and 1/150 gr. (0·43 mg.) of hyoscine. The infant was only slightly asphyxiated at birth and responded quickly to simple measures.

The placenta and membranes were delivered almost immediately. The babies were both males and weighed 5 pounds 11 ounces (2,580 g.) and 7 pounds (3,174 g.) respectively and both survived.

The Placenta and Membranes (Fig. 1)

These weighed 2 pounds 1 ounce (935 g.). The placenta was ovoid and 9 inches (22·9 cm.) in the longer diameter and 7½ inches (19 cm.) in the shorter one. The foetal

surface showed two cord insertions within ¾ inch (1·9 cm.) of each other and obvious anastomoses between their respective circulations could be seen in 2 places. The cords were entwined through 6 complete turns and the fatter cord had grooves in the surface of its Wharton jelly which accommodated the thinner cord. At no place did the placenta show any evidence of an amniotic partition.

Case No. 2 (4681). Aged 30 years

This patient was a multigravida, whose 3 previous pregnancies had ended in spontaneous normal delivery of living infants at term. There was no family history of twins on her side, but here also there were no less than 5 sets among the husband's near relatives. Twin pregnancy had been diagnosed clinically and radiologically at her first and only attendance at the 31st week. Labour commenced spontaneously at the 38th week and the cervix was fully dilated by the time of her admission, one and a quarter hours later, when the membranes were ruptured artificially at the vulva.

Spontaneous vertex delivery of the first baby—a male—occurred 40 minutes later. Immediately after this, the cord of the second foetus prolapsed and was found to be pulseless. There had been no noticeable fresh escape of liquor. Vaginal examination revealed a compound vertex presentation—a hand being below the head. Strong bearing down efforts achieved a quick spontaneous delivery of another male infant which required only minimal resuscitative effort. The placenta and membranes were delivered 10 minutes later to the accompaniment of a 3rd stage loss of 32 ounces (914 ml.).

The babies weighed 4 pounds 2 ounces (1,875 g.) and 4 pounds 9 ounces (1,846 g.) respectively and both survived.

At the end of the second week, however, the second baby developed cyanosis and, after repeated examinations and X-ray investigations, it was concluded that he had a congenital heart lesion. After 3½ weeks, he began to vomit his feeds and a palpable abdominal tumour was found and this proved at operation to be a hypertrophic pylorus. He survived the operation but is still under review as a case of congenital heart disease. His brother remained healthy throughout the neonatal period and continues to be in good condition, without any evidence of congenital malformation.

The Placenta and Membranes (Fig. 2)

The placenta and membranes weighed 2 pounds 9 ounces (1,136 g.). There was only one amniotic sac. There was no evidence of the remnants of a partition between the cords; indeed, the cords joined a common stem before reaching the placenta.

The cords were wound together spirally through 25 complete turns and there was one true knot of the cord of the first baby around that of the second, though there was no evidence that the latter suffered any constriction. The foetal surface of the placenta showed anastomoses between vessels which could be traced back through the common cord stem to the separate cords.

Case No. 3 (7310). Aged 31 years

This patient had had 1 previous normal delivery at term. She was referred for examination and booking at the 32nd week of pregnancy, when the uterus was tense and reached to the xiphisternum. Radiological examination at the 32nd week revealed the presence of twins, one of them being anencephalic. Definition was poor, however, because of hydramnios. The patient was so uncomfortable that she was admitted to hospital and, when rest brought no relief, the amniotic sac was tapped abdominally. This procedure was carried out in the X-ray department and radiographs were taken immediately before paracentesis so that the needle could be inserted on the side on which the anencephalic foetus was lying. Seventy ounces (1·98 litres) of clear liquor were withdrawn and considerable foetal activity was noted during the process. Further radiographs taken immediately afterwards showed that the foetuses had changed sides.

The patient was much more comfortable and 2 weeks later, as there had been no appreciable re-filling of the uterus, she was allowed to go home. She was readmitted at the 37th week when the hydramnios was again obvious and she went into labour at the 38th week. The membranes ruptured spontaneously when the cervix had reached full dilatation and vaginal examination then showed that the head of the normal foetus was leading. When the head was delivered, several loops of cord were found around the foetal neck and it was necessary to cut one loop. It was, however, impossible to unwind the loops because they were tied together in a knot at one point. Further action was rendered unnecessary because the patient bore down relentlessly and the first foetus was born despite the tension on the cord. It was stillborn and showed early maceration. The second foetus suffered from anencephalus and presented by the face but was delivered easily and quickly without there being any evidence of rupture of a second bag of membranes. It too, was stillborn but not macerated. Both foetuses were male and weighed 4 pounds 13 ounces (2,183 g.) and 4 pounds 1 ounce (1,842 g.) respectively.

Placenta and Membranes (Fig. 3)

There was a single placenta into which both cords were inserted and there were several obvious anastomoses between the two circulations. The cords were knotted together in three separate places. There was no evidence of amniotic membrane dividing the sac.

Case No. 4 (23737). Aged 24 years

This was a case of triplets which had been diagnosed radiologically at the 23rd week of pregnancy. Labour commenced spontaneously at the 31st week and after 2 hours a large bag of membranes appeared outside the vulva. This was ruptured artificially and a moderate amount of clear liquor escaped. Vaginal examination then showed that two hands were presenting through the almost fully-dilated cervix. Also within the cervix was an unruptured sac containing two tiny feet which were easily identifiable. The head in the ruptured sac was lying in the right iliac fossa but it was possible to bring it over the

FIG. 1
Cords and placenta from Case No. 1.

FIG. 2
Cords and placenta from Case No. 2.

FIG. 3
Cords and placenta from Case No. 3.

J.K.W.

brim quite easily. Forceps were then applied and the head was eased through the incompletely dilated but distensible cervix. A living female infant weighing 2 pounds 12 ounces (1,247 g.) was delivered and afterwards made good progress. During these manipulations, the second sac ruptured and released muddy brown liquor. The second foetus, was, therefore, presumed dead and both it and the third foetus, which was delivered without any further bag of membranes being encountered, were so small that their delivery is best described as manual removal from the uterus. They were both males and were macerated and weighed only a few ounces each.

Placenta and Membranes

One half of the placenta was a hard white infarct and into this were inserted the cords of the two macerated foetuses. The cords were not knotted or entwined and there was no sign of an amniotic partition. The other half of the placenta was normal and into it was inserted the cord of the living infant which had been separated from the other two by a membranous partition.

Case No. 5 (18560). Aged 25 years

This patient had had 3 previous normal deliveries at term. She was 26-weeks pregnant by dates when she aborted a twin pregnancy which, on inspection, proved to have been dead for a considerable time. The foetuses were both males, they had been in a single amniotic sac and their cords were closely entwined but not knotted. Unlike the other 4 cases, the mono-amniotic condition was not complete in that there was a fringe of membrane between the insertion of the 2 cords. It is doubtful whether this represented the remains of a partition which had once been complete and which had broken down or whether it indicated a primary defect.

Discussion

The factor which determines the development of the amnion is the embryo itself (Hertig and Rock, 1945; Hertig, 1945), since no otherwise normal ovum has yet been described in which an amniotic space has formed before ectoderm and endoderm are already apparent. If the germ disc splits before the formation of an amniotic sac the two embryos will result in the formation of two amniotic sacs. Therefore, in the case of mono-amniotic twins, the split in the germ disc must occur after the formation of the single amnion. The amnion forms during the seventh to thirteenth days after fertilization (Hertig and Rock, 1945; Marchetti, 1945), but occasionally as late as the twelfth day it may still be absent (Stieve, 1931), so it may be presumed that twinning in these cases does not take place before the seventh day. On the other hand, it must occur while the embryo still retains its capacity for forming two toti-potential halves, that is before the fourteenth day, when the germ disc first assumes a simple axial arrangement (Marchetti, 1945; Wilson, 1945).

From this information it is possible to deduce that di-amniotic twins form before the seventh day, mono-amniotic twins between the seventh and thirteenth days and conjoined twins after the thirteenth day.

The genetic endowment of uniovular twins is identical and it has been assumed that their developmental possibilities are, therefore, identical also. Anencephaly is a malformation with a strong genetic attachment and familial incidence (Malpas, 1937; Penrose, 1946; Record and McKeown, 1951), so that in uniovular twins both would be expected to be affected by it and cases of this kind have been recorded (Josephson and Waller, 1933).

In view of this, the third case reported here has a special significance for embryologists and those interested in malformations, because one of the foetuses was normal and one anencephalic, yet there was intercommunication between the two placental circulations and no amniotic partition. Litt and Strauss (1935) recorded the only other case of mono-amniotic twins in which one foetus was anencephalic. The factor causing anencephaly in these cases can hardly have been genetic (only one ovum was fertilized) and the factor did not operate until after the seventh day. During the time to which these case reports apply, the writer has encountered a case of anencephaly in one of di-amniotic, apparently uniovular twins, but unfortunately the foetuses were not examined for finger and palm prints, eye colour, iris pattern and blood groups and so the full criteria for a uniovular origin were not satisfied (Newman, Freeman and Holzinger, 1942; Morison, 1949). Morison (1949) described 2 cases in which these strict criteria were applied and in each of which only 1 twin had gross multiple congenital malformations. Record and McKeown (1951) provided statistical evidence based on sex ratios, which proves that some identical twins were among their 66 cases of twin pregnancies with 1 malformed foetus.

With intercommunication of the placental circulations it might be expected that malforma-

tions in the foetal circulatory system would be encountered, even up to the extreme condition of acardia. The second case here described is significant in this respect, as are the cases of Jeune and Confavreux (1948) and Nemecskay (1936) in both of which 1 twin had extensive malformations of the heart while the other twin was clinically normal and survived.

Since uniovular twinning and congenital malformations are both thought to result from delays and setbacks in the early development of the embryo, caused by environmental influences (Stockard, 1921; Arey, 1923b), it would be surprising that the combination is not more frequently met with, were it not for the fact that, in the vast majority of cases, the intra-uterine environment of the twin embryos is as identical as their inheritance.

Quigley in 1935 reviewed the literature of mono-amniotic multiple pregnancy, and found 123 contributions in eight languages during three and a quarter centuries. Most of the authors quoted by him are agreed about the extreme rarity of the condition and one goes so far as to say that it is given to no obstetrician to see more than one case in his lifetime. Quigley described the 109th authentic case and in the 20 years since that time there have now been added to the literature a further 33 cases making a total of 142 cases out of which only 31 have resulted in double foetal survival (Table I).

TABLE I

Date	Authors	No. of Cases	Foetal Salvage		Special Features
			Double Survivals	Single Survivals	
1935	Rucker	1	0	1	
1935	Litt and Strauss	1	0	0	1 foetus anencephalic.
1936	Nemecskay	1	0	1	1 foetus with gross cardiac anomalies.
1936	Frewer	1	0	1	Bifurcated cord. Double live birth. One foetus died 30 hours after birth.
1938	Elert	1	1	0	
1938	Huizenga	1	0	0	Abortion of macerated foetuses at 28th week.
1940	Rhenter and Bégule	1	0	0	
1940	Schrank	1	0	0	Abortion of fresh foetuses at 24 weeks.
1940	Devraigne	1	0	0	Common cord insertion.
1940	Parks and Epstein	1	1	0	
1942	Jones	1	0	0	
1942	Aigner	1	0	1	
1946	Acosta-Sison *et al.*	2	1	1	Double survival came from Caesarean section for eclampsia.
1947	Boyle and Richter	1	0	0	Foetuses died *in utero* during toxaemic episode at 31 weeks.
1947	Coulton *et al.*	2	2	0	
1947	Woodburn	1	0	0	Abortion of macerated foetuses at 20 weeks.
1948	Jeune and Confavreux	1	0	1	One foetus died at 2½ months of multiple congenital heart malformations. Situs inversus visceram.
1949	Delascio *et al.*	1	1	0	
1951	Mendel	1	0	1	
1952	King *et al.*	5	2	3	Elective Caesarean section in 1 of double survival cases.
1953	Hagood and Stokes	1	1	0	
1953	Henderson	1	1	0	
1954	Wilson (present communication)	5	2	0	One anencephalic in 1 pair. One cardiac anomaly and pyloric stenosis in another pair.

The paper recording one further possible case (that of Gyulay, 1937) has not been available to the author and is, therefore, omitted from the table.

The practical importance of mono-amniotic twinning is the high foetal mortality which results from the knotting and entanglement of the cords. The cord of the second twin, encircled by a knot in the cord of the first, has frequently been found to have suffered constriction during the descent of the first foetus. A cord tightly wound round the neck of the first baby has been clamped and cut to facilitate delivery and subsequently found to belong to the second. Valamentous insertion with its attendant hazards is also frequent. The foetal mortality is in fact approximately 70 per cent (Quigley). It is, therefore, not surprising that only 4 out of the 10 mono-amniotic babies in this series survived—rather is it surprising that the 4 babies were obtained from 2 pregnancies, that is, there were 2 cases of double foetal survival to add to the 29 previously recorded.

Summary

Five cases of mono-amniotic multiple pregnancy are described.

The embryological aspects of this form of twinning are discussed.

The embryological significance of congenital anomalies in one of uniovular mono-amniotic twins is stressed.

Attention is again drawn to the high foetal mortality associated with the condition.

A summary of recorded cases brings the literature up to date.

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Addendum

Since this paper was prepared, 6 further cases have been traced in the more recent literature (those of Charlton *et al.*, 1953; Alment, 1954; Hanes, 1954; and Conybeare, 1954). Eleven of the 12 infants in these cases survived the neonatal period.

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MONO-AMNIOTIC TWINS WITH ONE BLIGHTED

Case Report

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IT is difficult to estimate the incidence of mono-amniotic twins but they are probably not so rare as is generally supposed. A total of 151 cases has now been reported but some undoubtedly are not recognized whilst others, in which the presence of only one amnion is confirmed, are not considered sufficiently unusual to merit publication. King *et al.* (1952) collected 5 cases in 18 months at the City of New Orleans Hospital, giving an incidence of 1:1,000 pregnancies. This contrasts with other estimated incidences of 1:6,000 (Müller, 1889) and 1:60,000 (Rosenberg) as quoted by Quigley (1935).

The foetal prognosis in mono-amniotic twins is distressingly poor. In Quigley's 109 collected cases the foetal loss was 68 per cent while King *et al.* (1952), who collected 34 cases and added 5 of their own, reported a foetal loss of 44 per cent. Subsequently cases have been reported by Hagood and Stokes (1953) and Henderson (1953), in which both twins survived, and by Crouch (1954), in which both were lost.

The incidence of congenital malformations is high in mono-amniotic twins but the very high foetal loss is principally due to entanglement and knotting of the umbilical cords in the common amniotic sac. The condition can only be diagnosed after delivery of the first baby when no second bag of waters is apparent. In these circumstances the second twin should be delivered as soon as possible in case a knot round its cord has been tightened by the first delivery. This offers the only means of reducing the foetal mortality, for a study of the reported cases suggests that the second baby is often lost at the time of the first delivery.

The case of mono-amniotic twins reported below is of unusual interest in that one twin was blighted before viability but it was nevertheless responsible for the death of the other twin at the 36th week of the pregnancy.

CASE REPORT

A primigravida, aged 20 years, was booked at St. Helier Hospital antenatal clinic on 4th July, 1952, at 12-weeks pregnancy. She was normal in every respect but it was noted at her next attendance a month later that the uterus was enlarged to the size of 20 weeks. She attended regularly for routine examinations and remained well, no further inconsistencies being noted. At the 37th week she reported that movements had ceased a week previously. The foetus was presenting as a vertex R.O.L. with the head engaged and its size was consistent with the duration of pregnancy. No foetal heart sounds could be heard on auscultation. An X-ray (Fig. 1) showed a twin pregnancy with one foetus very much smaller than the other. A positive Spalding's sign was present in both twins.

Three days later the patient was admitted in labour. After a first stage of 20 hours 30 minutes and a second stage of 10 minutes she had a normal vertex delivery of the larger twin which was stillborn and macerated. With the next contraction she was delivered of the smaller twin which was a well preserved, flattened foetus papyraceus. There was no evidence of a second amniotic sac and the liquor, which was stained with old meconium, appeared to be normal in amount. The third stage was normal and the puerperium was quite uneventful.

The placenta (Fig. 2) was oval in shape, measured 8 inches (20 cm.) by 6 inches (15 cm.), and weighed 1 pound (0·39 kg.). The cord of the smaller foetus measured 24 inches (61 cm.) in length and was twisted tightly 4 times round the cord of the larger foetus which measured 18 inches (46 cm.). The two cords had a common eccentric placental origin and the umbilical vessels anastomosed freely. A single amnion and chorion was present and there were no partitional remnants to suggest that there had originally been two amniotic sacs.

The foetuses were both female and weighed 6 pounds 9 ounces (2·98 kg.) and 7¼ ounces (0·21 kg.) respectively. Their lengths (crown–heel) were 20 inches (51 cm.) and 9½ inches (24 cm.). Whilst the larger foetus showed obvious signs of maceration with peeling skin the foetus

FIG. 1

X-ray at 37 weeks showing twins with one blighted. The larger twin has a positive Spalding's sign also.

FIG. 2
Mono-amniotic twins with placenta and membranes.

D.B.W.

papyraceus had a flattened, firm body and the skin was smooth. An autopsy showed no congenital malformations in either twin and the findings were compatible with death from intra-uterine asphyxia.

Comment

It is exceptionally rare for one of mono-amniotic twins to be blighted in mid-pregnancy whilst its co-twin continues to develop, both being expelled near term. Only 3 such cases have previously been recorded (Kindred, 1944) and in none of these was cord entanglement the apparent cause of the death of the blighted twin. Similarly in the case described above it seemed more likely that circulatory reversal through the placental anastomosis by the stronger twin had caused the death of its fellow. If cord knotting sufficient to kill one foetus had occurred at this stage it is probable that the other would have died also. It is clear, however, that the death of the larger twin was caused by the tight constriction of its cord by the abnormally long cord of the retained blighted twin. Each was thus responsible for the other's death though by a different mechanism.

It is of particular interest that the blighted twin was flattened and relatively unmacerated despite the single amniotic sac for this cannot be explained by current theories on the formation of a foetus papyraceus. According to Kindred (1944) and Mills (1949), when liquor in the sac of the blighted twin is deficient or absorbed, maceration is arrested and the foetus is subjected to compression by the intact sac of the healthy twin which produces a foetus papyraceus. These conditions do not occur in a blighted mono-amniotic twin which is still bathed in liquor and is not subjected to compression until the other twin has grown appreciably. Possibly by an anomaly of the circulatory anastomosis it is subjected to progressive exsanguination and dehydration which delays maceration. Later it must be flattened by pressure from the larger foetus though it is apparent from the X-ray (Fig. 1) that by the 37th week it has escaped from direct pressure and presumably has moved about so freely that cord entanglement and another intra-uterine death have resulted.

Summary

A case of mono-amniotic twins is recorded in which one twin was blighted in mid-pregnancy and subsequently caused the death of the other twin at the 36th week by cord entanglement.

I should like to express my thanks to Miss Eileen Wilson for permission to publish this case.

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A SIMPLE APPARATUS FOR RESUSCITATION OF THE NEWBORN

BY

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THIS is a description of a simple apparatus that has been successfully used for the giving of automatic artificial respiration to newly born asphyxiated babies. It has also been used for expanding the lungs during thoracic operations in the newborn.

The apparatus is easily constructed from two glass T-tubes, Penrose tubing, a catheter and a rubber glove or rubber bag (Fig. 1).

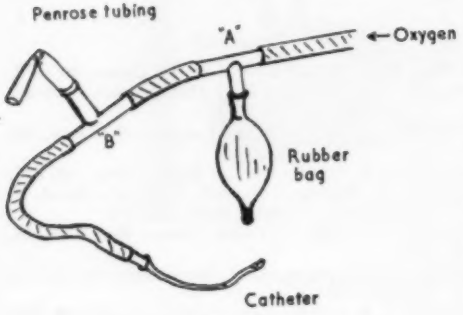

FIG. 1

The one limb of the T-tube "A" is connected by rubber tubing to an oxygen cylinder with pressure gauge. The rubber glove or rubber bag (the inner rubber balloon of a small football—one litre capacity—is also useful) is attached to the other limb of the T-tube "A". This T-tube is now connected by a short length of rubber tubing to the T-tube "B". The stem of this T-tube is held almost vertical (at an angle of about 80°) using a cardboard box or plaster of Paris bandage for support. Penrose tubing about 7 cm. long and ½ cm. wide (or a finger-stall with a hole cut in its end) is fixed on to this vertical limb of the T-tube. The other limb of the T-tube is attached by a suitable length of rubber tubing to a thin rubber catheter (e.g., No. 11F) or a No. 0 endotracheal tube.

The apparatus works on the following principle. The catheter is placed in the nose (or trachea) of the baby. The rubber bag is filled with oxygen. Due to its elasticity the bag acts as a source of positive pressure, forcing oxygen through the catheter and so expanding the lungs and producing "inspiration". As soon as the pressure in the system reaches a certain pressure (about 15 cm. water) the Penrose tubing valve, which is folded on itself, opens so causing the bag to collapse and thereby collapse of the lungs and "expiration". This valve also acts as a safety valve, preventing excessive pressures being built up and overdistension of the lungs. Varying the length of the Penrose tubing produces a change of effective positive pressure and rate of artificial respiration. By running oxygen in constantly at 7 litres per minute this cycle of inspiration and expiration is continually repeated.

The length of catheter placed in the nose, in order that the tip lies just above the entrance to the trachea, is the distance measured from the tip of the nose to the tragus of the ear. This point on the catheter can be permanently marked. The mouth is closed by the thumb and forefinger of the operator or with a strip of adhesive tape to prevent escape of too much oxygen.

As soon as the mouth, pharynx and nose have been cleared of foreign material by suction the catheter is put into the right or left nostril and the oxygen turned on. If an anaesthetist is available (e.g., at Caesarean sections) the

catheter may also be passed intra-tracheally first, the trachea sucked out and then the catheter attached to the apparatus.

The advantages of this apparatus are that it is simple and suitable for use by a nurse; it is automatic; the artificial respiration produced simulates closely the breathing of a newborn baby which has an irregular and rapid respiration of about 40 per minute; it is safe as no over-distension of the lungs can occur; the apparatus is simple to make; it saves time when emergency oxygenation is needed.

SOME ASPECTS OF BREECH DELIVERY

BY

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THE importance of any obstetric abnormality depends, among other factors, upon the frequency with which it is encountered and the risk it presents to the foetus and to the mother. Breech delivery demands consideration on both these scores since not only is it relatively common but the associated foetal mortality remains disconcertingly high. This is borne out by the fact that analysis of 1,307 single uncomplicated breech deliveries conducted in a number of British hospitals between 1948 and 1952 revealed a foetal mortality of 11·4 per cent; a figure equal, to all intents and purposes, to that of 12·0 per cent quoted by Bourne and Williams (1945) nearly 10 years ago.

This high rate of loss lends importance to any series of cases where the outcome is less disappointing. It is for this reason that the results of breech delivery in University College Obstetric Hospital are being reviewed, since, during the past 5 years, the foetal mortality has been reduced to and maintained at a low level.

THE CHOICE OF THE METHOD OF DELIVERY

The present series covers the period 1949 to 1953 inclusive and consists of 136 patients—92 primiparae and 44 multiparae—in whom a single infant presented by the breech at the time of delivery. Vaginal delivery was allowed in 118 of these cases—79 primiparae and 39 multiparae—an overall incidence of 86·7 per cent while Caesarean section was considered necessary in 18 patients—13 primiparae and 5 multiparae—an incidence of 13·3 per cent. The fact that 16 of these operations were elective shows that this method of delivery was decided upon during pregnancy in a relatively large proportion of cases.

Caesarean section

This course is justifiable only if there is reason to believe that vaginal delivery would have seriously prejudiced the chances of the infant's survival. This point is best judged by considering the main indications for operation which were: disproportion in 7 cases, elderly primiparity in 6 and a bad obstetric history in the remaining 3.

Disproportion. In the presence of disproportion the foetal risk of breech delivery is extremely high (Caldwell and Studdiford, 1929; Gordon *et al.*, 1934; Lowrie, 1939; Seeley and Siddall, 1940; Diddle *et al.*, 1942; Moore and Steptoe, 1943; Cox, 1950; Brown and Irvine, 1951). The management of these cases is complicated by the fact that only rarely may a trial of labour safely be allowed. Although this course has been recommended both by Marshall (1934) and Cox (1950), it should be undertaken solely with the object of confirming or excluding disproportion and not with the aim of reducing the diameters of the foetal head to an extent necessary to negotiate the maternal pelvis. For this reason Caesarean section is the treatment of choice in the presence of frank disproportion since only by this means may the trauma inseparable from a vaginal breech delivery be avoided.

In the present series, disproportion was encountered in 7 cases—5 primiparae and 2 multiparae—all of whom were delivered by elective Caesarean section. In a further 2 cases, both primiparae, disproportion was suspected although unproven. Management here was by trial of labour which succeeded in one patient, the outcome being an assisted breech delivery, but failed in the other where a combination of incoordinate uterine action and failure of the breech to engage led to Caesarean section being

performed after labour had been in progress for 12 hours.

Elderly Primiparity. The relation of age to foetal mortality, mentioned by Gordon *et al.* (1934) and Racker (1943), has been variously ascribed to foetal anoxia (Walker, 1954) or to a greater incidence of uterine inertia and operative deliveries in the more elderly (Walsh and Kuder, 1944; Baird, 1952). On the other hand, where vaginal delivery is allowed in such patients this is frequently uneventful (Neilson and Neilson, 1954).

A decision in favour of Caesarean section in the elderly primipara thus often depends upon factors other than age alone, such as the length of time married, the attitude towards labour and the degree of concern for the safety of the infant.

In the present series there were 10 otherwise normal primiparae over 35 years of age. In 6 of these an elective Caesarean section was carried out, the remainder being allowed a vaginal delivery. In view of the fact that in this latter group labour was invariably straight-forward, it may be argued that this course should have been more widely adopted. Although it is impossible to be definite on this point it is reasonable to suggest that a trial of uterine action might have been allowed in a greater number of cases, operation being resorted to in the event of any abnormality arising in the course of labour.

Past Obstetric History. Of the 44 multiparae in the present series, 22 gave a history either of one or more stillbirths or neonatal deaths or of a previous operative delivery. Owing to the presence of disproportion, an elective Caesarean section was carried out in 2 of these patients. In the majority of the remainder, in whom the nature of past complications rendered improbable their recurrence in any future labour, a vaginal delivery was allowed.

In 2 cases, however, where death of the foetus had occurred in the course of a previous labour, the patient's concern for the safety of her infant was such that Caesarean section was felt to be the treatment of choice. In a further case, where section had previously been carried out because of cervical dystocia, it was also considered best to repeat this operation.

Vaginal Breech Delivery

As already stated, a vaginal breech delivery was allowed in a total of 118 cases—79 primiparae and 39 multiparae. These patients have been divided into three groups depending upon whether delivery was spontaneous, assisted or completed by extraction (Table I).

Spontaneous Breech Delivery. This may be defined as a breech delivery taking place without external aid of any kind. As shown in Table I, this group consisted of only 7 cases. In 2 of these the malpresentation was undiagnosed while in the remainder the infant was premature, foetal death having occurred before the onset of labour in 2 instances.

The danger in these cases is that, delivery being inevitably rapid, the risk of intra-cranial trauma is considerable, the more so since the infant is usually premature.

Breech Extraction. This implies formal extraction of the breech under general anaesthesia. Although recommended by some American obstetricians as the method of choice in all breech deliveries (Piper and Bachman, 1929; Goethals, 1936; Seeley and Siddall, 1940; Potter *et al.*, 1945; Vogt *et al.*, 1945), such a view has never been accepted in this country, owing to the belief that the necessary manipula-

TABLE I

*Types of Vaginal Breech Delivery**

	Total Cases	Spontaneous	Extracted	Assisted
Primiparae	79	6 (7·6)	9 (11·4)	64 (81·0)
Multiparae	39	1 (2·6)	1 (2·6)	37 (94·8)
All Cases	118	7 (5·9)	10 (8·5)	101 (85·6)

* In this, as in subsequent Tables, figures in parentheses indicate percentage incidence.

tions greatly increase the risk of foetal trauma.

In the present series a breech extraction was performed in 10 cases—8·5 per cent of vaginal breech deliveries—being undertaken only upon such indications as foetal distress, maternal distress and delay in the second stage of labour.

Assisted Breech Delivery. Here delivery is largely completed by the maternal efforts, assistance being confined as a rule to the birth of the arms and of the head. The advantages of this type of delivery are that, while the amount of manipulation of the infant is relatively slight, the dangers presented by a rapid and uncontrolled delivery are avoided. In consequence the risk of trauma is reduced to a minimum.

For these reasons an assisted breech delivery was aimed at whenever practicable in the present series; the proportion of cases thus managed being 85·6 per cent of all vaginal breech deliveries.

Foetal Mortality and Morbidity

The gross foetal mortality in the series under consideration was 12·5 per cent—16 infants being lost. Of these, 7 died *in utero* before labour, 3 possessed congenital abnormalities incompatible with life and 5, all of whom weighed under 1,500 grammes, were lost during the neonatal period. In this last group, post-mortem examination showed that death in every case was due to prematurity, birth trauma playing no part.

There remained 1 infant stillborn after an assisted breech delivery. Autopsy revealed a tentorial tear and haemorrhage around the brain-stem. This was the only case where death was directly attributable to trauma sustained at delivery.*

In assessing the intrinsic risk of breech delivery, allowance is usually made for various factors which may affect the chances of the infant's survival. Although no hard and fast rules for such a computation exist, it would seem that any true estimate of this risk should be reached by excluding none but those cases where it is certain that labour played no part in causing the death of the infant. Thus, in the present series, only the following cases should be excluded in calculating the corrected foetal mortality:

1. Intra-uterine death before the onset of labour.
2. Congenital malformations incompatible with life.
3. Gross prematurity—infants under 1,500 grammes birth weight—since all deaths under this weight were attributable to prematurity.

As shown in Table II, the corrected foetal mortality after excluding all such cases was 1·0 per cent.

The fact that only 1 infant was lost forbids any attempt to assess on the basis of foetal mortality either the relative risks of the three types of vaginal breech delivery referred to earlier or the merits of the various procedures used in the course of labour. Information on these points was therefore sought by considering the condition of the infant at birth—assessed as either "poor" or "good or fair"—since this was felt to be directly related to the safety of the delivery. Table III shows the effect of the type of breech delivery on the condition of the infant at birth. Although the numbers involved are small, they suggest that, as might be expected, assisted breech delivery carries the least risk to the infant while breech extraction, possibly owing in part to the complication necessitating such intervention, presents the greatest dangers.

The Technique of Assisted Breech Delivery

From the point of view of the effect on the infant of the various procedures employed in delivery, the greatest amount of interest attaches to those used in assisted breech deliveries. This is partly due to the fact that these cases constitute by far the largest group—85·6 per cent of all vaginal breech deliveries—and partly because the foetal risk both in extraction and in spontaneous breech delivery is to a large extent beyond the control of the obstetrician.

Of 87 assisted breech deliveries, 61 were

* Case Number 49/5. Primigravida, aged 24. Mild pre-eclampsia in late pregnancy. Maximum Blood Pressure 140/90. Spontaneous onset of labour. First stage of 11 hours, second stage of 1 hour. Assisted breech delivery, arms extended, brought down by Løvset's manœuvre, head delivered by Burns-Marshall manœuvre. Local anaesthesia only for delivery. Breech undiagnosed before the onset of labour. No pelvimetry.

TABLE II

The Corrected Foetal Mortality in Vaginal Breech Delivery

	Total Cases	Deaths	Survived	Per Cent Died
Primiparae	73	1	72	1·4
Multiparae	27	0	27	—
All Cases	100	1	99	1·0

TABLE III

The Relation of the Condition of the Infant at Birth to the Type of Breech Delivery

	Total Cases	Condition "Poor"	Condition "Good or Fair"	Per Cent "Poor"
Spontaneous breech delivery	3	1	2	33·3
Assisted breech delivery	87	16	71	18·4
Breech extraction	10	4	6	40·0
All Cases	100	21	79	21·0

carried out in primiparae and 26 in multiparae. Sixteen (18·4 per cent) of the infants delivered were considered to be in a "poor" condition at birth—11 (18·0 per cent) from primiparous and 5 (19·2 per cent) from multiparous deliveries. Of these infants, 1 was stillborn, the remaining 15 recovering after treatment.

In these deliveries four procedures in particular were widely employed, namely:

1. Episiotomy.
2. The delivery of extended arms by Løvset's manœuvre.
3. The administration of a general anaesthetic for the birth of the arms and of the head.
4. The application of the forceps to the after-coming head.

Episiotomy. The importance of an episiotomy in breech delivery is too widely realized to require more than passing comment. According to Baxter (1949), the value of the procedure lies in the fact that it increases the ease of the delivery of the breech itself, allows room for any subsequent manipulations and reduces the risk of compression of the after-coming head. In view, however, of the fact that in the present series an episiotomy was performed in virtually every case—100·0 per cent of primiparae and 88·5 per cent of multiparae—it is impossible to test the validity of these views in relation to the condition of the infant at birth.

Løvset's Manœuvre. The principal advantage of this manœuvre, first described by Løvset (1937) and reported upon favourably by Greig (1945), Trites (1948), Ingerslev (1949) and Newton (1949), is that the amount of manipulation of the infant is considerably less than where other methods are used to bring down extended arms. In addition, as the foetal back is kept anterior throughout, the risk of an occipito-posterior position of the after-coming head is, if not entirely eliminated, certainly greatly reduced.

In the present series of assisted breech deliveries the arms were delivered spontaneously, being already flexed, in 45 cases—30 primiparae and 15 multiparae—and were extended in 42 cases—31 primiparae and 11 multiparae. In this latter group Løvset's manœuvre was the procedure of choice in 86·1 per cent of primiparae and 84·6 per cent of multiparae, an overall incidence of 85·7 per cent. The proportion of infants "poor" at birth where the arms were extended was 19·4 per cent as against 15·8 per cent where the arms were delivered spontaneously. Owing to the inevitably greater possibility of foetal trauma in association with extended arms, this finding should not suggest that Løvset's manœuvre is unduly hazardous. The only means whereby this could be shown would be by comparison with the results obtained

from other methods for the delivery of extended arms. The infrequency with which such alternative procedures were adopted in the present series renders any such comparison impossible.

General Anaesthesia. Of the 87 cases under consideration, 42—36 primiparae and 6 multiparae—received a general anaesthetic for the delivery of the arms and the head. The yearly proportion of cases thus managed is set out in Table IV.

TABLE IV

The Yearly Percentage Incidence of General Anaesthesia in Assisted Breech Deliveries

Year	Primiparae	Multiparae	All Cases
1949	26·7	—	18·2
1950	37·5	—	25·0
1951	50·0	33·3	42·9
1952	71·4	25·0	61·1
1953	93·8	60·0	85·7
All Years ..	59·0	23·1	48·3

Theoretically, there are two main reasons why general anaesthesia should be of value in assisted breech deliveries. In the first place, the necessary manipulations, owing to the complete analgesia provided, are more easily and hence more gently carried out. Secondly, unforeseen difficulties may arise in connexion with the delivery of the arms and the head. If the patient is conscious much time may be wasted and the foetus undergo severe oxygen depletion while the anaesthesia necessary for the management of these difficulties is induced. This danger may be avoided if a general anaesthetic is started immediately after the birth of the breech and trunk, the more so if induction is rapid and smooth and good oxygenation maintained (Law and Ransom, 1954).

If these arguments are correct, it might be expected that those cases receiving a general anaesthetic would show a smaller incidence of infants "poor" at birth than where this measure was omitted. It will be seen from Table V that this was to some extent the case although the difference, possibly owing to the small numbers involved, is not significant.

The Application of Forceps to the After-coming Head. Although this procedure originally described by Smellie (1752) and greatly amplified by Baudelocque (1789), is still not in general use as a routine measure, it is widely recognized as of the greatest value whenever difficulties arise at this stage of delivery (Moore and Steptoe, 1943; Lowrie, 1939; Tompkins, 1943; Baxter, 1949; Zacharias and Heery, 1950; Noble *et al.*, 1951; Arnot and Nelson, 1952; Ware and Roberts, 1954). Its advantages are that traction is made directly upon the foetal head, thus eliminating the risk of injury to the cervical spine; that flexion can be easily and safely maintained and that the rate of descent and delivery of the head can be accurately controlled, thus preventing it from slipping too rapidly over the perineum and undergoing a dangerously sudden release of pressure.

The incidence of the application of forceps to the after-coming head in the 87 assisted breech deliveries under review is set out in Table VI, while Table VII, in which the yearly incidence of this procedure is considered, shows that its use has recently been greatly extended.

Thus, although the overall incidence of forceps application was only 43·7 per cent—52·5 per cent for primiparae and 23·1 per cent for

TABLE V

The Relation of General Anaesthesia to the Condition of the Infant at Birth: Assisted Breech Deliveries

	Anaesthetic Given		No Anaesthetic Given	
	Total Cases	Number "Poor" at Birth	Total Cases	Number "Poor" at Birth
Primiparae	36	5 (13·9)	25	6 (24·0)
Multiparae	6	1 (16·7)	20	4 (20·0)
All Cases	42	6 (14·3)	45	10 (22·2)

TABLE VI

The Application of Forceps to the After-coming Head

	Total Cases	Forceps Used	Forceps Not Used	Per Cent Forceps
Primiparae	61	32	29	52·5
Multiparae	26	6	20	23·1
All Cases	87	38	49	43·7

TABLE VII

Yearly Percentage Incidence of Forceps to the After-coming Head: Assisted Breech Deliveries

Year	Primiparae	Multiparae	All Cases
1949	20·0	14·3	18·2
1950	12·5	—	8·3
1951	25·0	16·7	21·4
1952	78·6	25·0	66·7
1953	93·8	60·0	85·7

multiparae—this rose in the last 2 years of the period under survey to 76·9 per cent—86·7 per cent for primiparae and 44·5 per cent for multiparae.

If the arguments in favour of this procedure are valid, it might be expected that where it was employed the condition of the infant at birth would be better than where the after-coming head was delivered by other methods. This, however, was not the case, the proportion of infants "poor" at birth being 23·7 per cent where the forceps were used as against 14·3 per cent where other methods were practised.

Although, owing to the small numbers involved, no definite conclusions can be drawn from these figures, two possible explanations may be put forward. In the first place it may be argued that the forceps do not possess any advantages over other methods for the delivery of the after-coming head. This view gains support from the fact that several obstetricians, notably Hansen (1941), Dieckmann (1946) and Arnot and Nelson (1952), have obtained excellent results while rarely resorting to the forceps. Alternatively, it is possible that since the forceps were not used in the present series to the exclusion of all other methods, they may well have been employed in a higher proportion of difficult deliveries in which the condition of the infant at birth would necessarily be less satisfactory.

There is much evidence in favour of such an explanation. In certain cases the forceps were applied without preliminary anaesthesia. This suggests sudden difficulties and the need to avoid all waste of time in completing the delivery. There were only 5 such cases, but in 3 the condition of the infant gave rise to concern. If only cases where an anaesthetic was given prior to the application of the forceps are considered, comparison of these cases with those where this procedure was not carried out shows the proportion of infants "poor" at birth to be the same in both groups (Table VIII).

Study of the case notes showed that the group of cases receiving a general anaesthetic included several where anaesthesia was induced for the application of forceps only after unsuccessful attempts at delivery by other means. Even in the presence of such difficulties the overall condition of the infants delivered with the forceps was as good as that following straightforward labours requiring no such management. This being so, the sequence "planned anaesthetic—forceps to the after-coming head" strongly suggests itself as the method of choice in all assisted breech deliveries.

Further evidence in favour of this procedure was obtained by dividing the years under survey into two periods: 1949 to 1951 and 1952 to 1953. During the first 3 years the sequence "general anaesthesia—forceps" was rarely resorted to, delivery usually being effected by other means, while in the last 2 years this tendency was reversed. Comparison of the condition of the infants born during these two periods shows that in the first the proportion of infants "poor" at birth was 20·8 per cent—22·6 per cent for

TABLE VIII

The Condition of the Infant at Birth in Relation to General Anaesthesia followed by Forceps to the After-coming Head

	Forceps and Anaesthesia		Remainder	
	Total Cases	Condition at Birth "Poor"	Total Cases	Condition at Birth "Poor"
Primiparae	29	5 (17·2)	32	6 (18·8)
Multiparae	4	1 (25·0)	22	4 (18·2)
All Cases	33	6 (18·2)	54	10 (18·5)

primiparae and 17·7 per cent for multiparae—as against 15·8 per cent—13·3 per cent for primiparae and 25·0 per cent for multiparae—in the second (Table IX).

TABLE IX

Comparison of the Periods 1949 to 1951 and 1952 to 1953 from the Standpoint of the Condition of the Infant at Birth

	Incidence of Condition "Poor" at Birth (Per cent)		
	Primiparae	Multiparae	All Cases
1949–1951 ..	22·6	17·7	20·8
1952–1953 ..	13·3	25·0	15·8

Bearing in mind that the increase in the use of general anaesthesia and forceps took place largely in primiparae (Tables IV and VII), the above findings suggest that the improvement in the condition of the infant at birth during the last 2 years may well have been due to the extended use of general anaesthesia coupled with the application of the forceps to the after-coming head in assisted breech deliveries.

SUMMARY

(1) The results of 136 cases where a single infant presented by the breech at the time of delivery have been reviewed.

(2) Of these cases, 118 were delivered vaginally—86·7 per cent—of which 79 were primiparae and 39 multiparae.

(3) The Caesarean section rate was 13·3 per cent. The main indications for operation were: disproportion, elderly primiparity and a bad obstetric history.

(4) After allowance was made for intrauterine deaths before the onset of labour, congenital abnormalities incompatible with life and infants under 1,500 grammes birth weight, the corrected foetal mortality for vaginal breech deliveries was 1·0 per cent.

(5) Of the vaginal breech deliveries, 5·9 per cent were spontaneous, 8·5 per cent were breech extractions and 85·6 per cent were assisted breech deliveries. This last-named procedure has many advantages over both other types of breech delivery.

(6) Of the various techniques employed in assisted breech delivery, the administration of a general anaesthetic after the birth of the breech and trunk and the application of the forceps to the after-coming head were most often used. The proportion of cases thus managed showed a steady yearly increase.

(7) Evidence is presented that these two procedures play an important part in reducing the amount of trauma associated with breech delivery and, in consequence, should together be considered as the method of choice in the management of assisted breech delivery.

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AN UNUSUAL CASE OF BLOOD DISEASE IN PREGNANCY

BY

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SEVERAL reports have appeared in recent months in the literature of incoagulability of blood associated with severe accidental ante-partum haemorrhage. It has long been realized that certain patients with accidental haemorrhage were prone to severe post-partum haemorrhage, while in others the third stage caused no concern. The first mention of this complication was over fifty years ago when DeLee (1901) postulated a haemophilia-like condition of the blood of a patient dying of severe accidental haemorrhage, and in 1936 Dieckmann associated the condition with a low fibrinogen concentration in the blood. It was not until 1949 that the therapeutic effect of giving fibrinogen by intravenous injection was tried out by Moloney and his colleagues, and in 1950 Weiner and his coworkers showed that there was a definite afibrinogenaemia correctable by the intravenous injection of fibrinogen.

Since then various cases of severe accidental ante-partum haemorrhage associated with afibrinogenaemia have been reported, mostly from America but a few reports have come from the Continent, and very recently three reports have appeared in the British literature (Moore, 1954; Barnett and Cussen, 1954; Feeney, 1954). The case reported by Moore was not recognized until post-partum haemorrhage occurred and in the discussion the comment is made that the diagnosis should be possible before delivery. We present the following case which was diagnosed prior to delivery, in the belief that it shows several interesting features relevant to the early diagnosis of the condition.

The patient, a primigravida of 36 years, had been married for 13 years. She had had no serious illnesses but for the past 5 years she had been taking thyroid gr. i. daily, originally started in an effort to lose weight.

The last menstrual period was in November, 1953 and antenatal care was carried out by the general practitioner. On the 2nd June, 1954 the patient had a wisdom tooth extracted under local anaesthesia. This was followed by fairly severe facial pain but very little haemorrhage. For the pain the patient took aspirin tablets gr. 5 to a total of 6 a day for 6 days, i.e., approximately 180 gr.

On 9th June, the patient awoke about 4 a.m. and found she was bleeding *per vaginam* and also from her tooth socket. She had some right sided abdominal pain. Her blood pressure at 6.20 a.m. was 90/60 mm. Hg. Morphia gr. ¼ was given and the patient transferred to hospital.

On admission at 7.15 a.m. the patient was pale, slightly shocked and bleeding orally and vaginally. There were no petechiae but haematomata appeared round each needle puncture. Her pulse was 108/min. B.P. 130/80 mm. Hg. She had no oedema but there was a cloud of albumen in a catheter specimen of urine.

The uterus was the size of a 32-weeks gestation. It was woody hard, but not tender. No foetal parts could be felt and no foetal heart heard. Blood was taken for grouping and cross-matching and a dextrose intravenous drip was commenced soon after admission. At 9 a.m. the patient was vomiting blood and had a fairly heavy vaginal loss. Her B.P. was 110/70 mm. Hg, the pulse 100/min. and the first pint of blood transfusion was started. As it was noted that the blood in a plain tube was not clotted after 2 hours the possibility of fibropenia was entertained and reconstituted fibrinogen 145 mg. in 10 ml. saline was given intravenously.

By 4 p.m. the patient had received 5 pints of blood, 3 being less than 24 hours old and also a further intravenous injection of fibrinogen (145 mg.). Her estimated loss was about 5 pints and the tooth socket had ceased to bleed.

She was complaining of uterine contractions and a vaginal examination was made. The cervix was found to be half dilated and the forewaters were ruptured, a small head descending into the pelvic cavity. Vaginal bleeding ceased and labour progressed normally.

At 6.25 p.m. the cervix was fully dilated and a low forceps delivery of a stillborn foetus weighing 3 pounds was performed under local anaesthesia. Ergometrine 0·5 mg. was given at the time of delivery of the anterior shoulder and the placenta was delivered immediately with about 20 ounces of old and fresh blood. This was followed by a trickle of bright red blood, which was partially due to a vaginal tear. This was sutured with

control of the bleeding. The total loss at delivery was estimated at 40 ounces and the patient's blood pressure was 95/70 mm. Hg. A pint of fresh blood was therefore transfused in 10 minutes.

By 9 p.m. the transfusion of the 9th pint of blood was commenced. The patient had lost a further 40 ounces despite the fact that the uterus was firmly contracted. In view of this a general anaesthetic was given and the vagina explored. No laceration was found and the uterus was packed with difficulty owing to the firm contraction which was maintained throughout the manipulation. The bleeding was controlled by the pack. Transfusion was continued overnight and a further fibrinogen injection given after packing the uterus. The pack was removed 12 hours later without further loss. Total blood given was 11 pints and the total loss was approximately 9 pints.

The patient's subsequent progress was complicated by pelvic sepsis and venous thrombosis, but no further bleeding occurred.

Pathological Investigations

9th June, 1954. On admission. Haemoglobin 94 per cent. Platelets abundant. Fibrinogen present. Bleeding time 4 minutes 30 seconds. Blood collected in a dry tube failed to clot. 9 p.m. Clotting time 9 minutes.

10th June, 1954. Haemoglobin 72 per cent. Clotting time 5 minutes.

11th June, 1954. Blood collected in a dry tube clotted immediately but after 30 minutes the clot had partially fragmented.

18th June, 1954. Haemoglobin 70 per cent. W.B.C.'s 18,400 per c.mm. Reticulocytes 5 per cent. Platelets abundant. Plasma fibrinogen 0·35 g./100 ml. Prothrombin Index 100 per cent.

Discussion

It is surprising that so little notice of this complication of accidental ante-partum haemorrhage has been taken in this country until so very recently. Since Weiner and his co-workers (1950) reported the results of their investigation into the cause of this condition a number of case reports have been published in America and a few on the Continent, and now 4 cases have been reported in Great Britain. The condition is also given brief mention by Biggs and Macfarlane in their recent book on blood coagulation (1953).

The first serious effort to find the cause of this condition was made by Weiner and his co-workers and the results were published in 1950. They found that in certain cases of accidental ante-partum haemorrhage there was a defect in the coagulation mechanism and that the changes were characterized primarily by a decrease in fibrinogen concentration, but that there was also some decrease in prothrombin activity and in some cases a circulating fibrinolysin was present. They noted that these changes only occurred in severe cases of accidental ante-partum haemorrhage but that the condition could be diagnosed by the repeated observation of the clot formed by the patient's blood. In 2 of the patients studied the blood coagulating mechanism was normal prior to the accidental ante-partum haemorrhage suggesting that the fibrinogenaemia was secondary to the accidental ante-partum haemorrhage and not the cause.

About the same time Schneider (1950) showed that in rabbits placental extracts produced first a hastening of coagulation and later a delay and he was able to identify the toxic principle as thromboplastin. He produced similar results by traumatizing the placental site. Page, Fulton and Glendenning (1951) published their results of the effect of the intravenous injection of placental thromboplastin in dogs and the study of 6 cases of accidental ante-partum haemorrhage. They concluded that defibrination is probably due to the escape of placental or decidual thromboplastin into the maternal circulation. This converts the prothrombin to thrombin which in turn converts the fibrinogen to fibrin and the latter is deposited over a very large vascular area, but may sometimes be the cause of severe visceral lesions. The rate of the fibrinogen depletion was measured in minutes, whereas if it were due to a fibrinolysin it would be a much slower process. The presence of a fibrinolysin in some cases was due, they postulated, to a repair mechanism developing after the initial injury, for the purpose of removing deposited fibrin and repairing the damage done by the action of the thromboplastic proteins. In 1953, in a further communication, they showed by means of radioactive extracts that most of the thrombin was deposited in the liver, lungs and spleen.

In 1952 Schneider published a method for the rapid evaluation of fibrinopenia which he claimed aided in the diagnosis of the condition, but the simple observation of a sample of venous blood incubated at 37° C. seems to give adequate information. If the freshly drawn venous blood fails to clot or form a normal

sized stable clot it indicates a critical level of circulating blood fibrinogen and if the clot dissolves within an hour the haemostasis is inadequate. This dissolution of the clot which was originally thought to be due to a fibrinolysis Weiner, Reid and Roby (1953) now believe to be due solely to low blood fibrinogen (100–150 mg. per cent).

It was the absence of clotting in blood taken for cross matching and the presence of oral bleeding that made us suspect a blood dyscrasia and realize we were not dealing with a simple ante-partum haemorrhage in our case. It was also noted that each venepuncture wound and injection site continued to ooze for many minutes. Owing to the kind help of Dr. Tovey of the South Western Regional Blood Transfusion Service we were able to obtain human fibrinogen for intravenous injection and the first ampoule was given with the first pint of blood. Not having had previous experience in the use of therapeutic fibrinogen we failed to give an adequate dose early on, and, although 290 mg. of fibrinogen and 4 pints of blood controlled the oral bleeding, it did not prevent a severe post-partum haemorrhage. It seems probable that the further injection of fibrinogen did more in stopping the bleeding than did packing the uterus.

The sudden onset of bleeding from a tooth socket that had not bled for 6 days was one of the interesting features of our case. That the oral bleeding occurred almost simultaneously with the vaginal bleeding seems to confirm the view that the incoagulability of the blood follows the accidental ante-partum haemorrhage and is not the cause of the condition. Weiner suggests that artificial rupture of the membranes by decreasing intra-uterine pressure, may prevent the further dissemination of placental thromboplastin and thus arrest the defibrination. We certainly found that our patient's condition improved after the membranes were ruptured but the subsequent post-partum haemorrhage showed that the fibropenia was still uncorrected.

In reviewing the case the role of aspirin was considered. This drug is known to be capable of reducing prothrombin to a level sufficient to cause abnormal bleeding and the amount this patient had taken during the week prior to admission may possibly have been a complicating factor in this case. However, the pathological findings fitted in much better with an afibrinogenaemia than with a reduction of prothrombin.

In spite of the relative infrequency of this complication of accidental ante-partum haemorrhage it must have been the cause of death in numerous cases which were attributed solely to haemorrhage and shock. If this possibility is kept in mind in all cases of severe accidental ante-partum haemorrhage an early diagnosis can be made. The freshly drawn venous blood should be examined for clot formation and for clot fragmentation when incubated at 37° C. If the first sample clots normally fresh samples should be examined at hourly intervals as the defibrination occasionally does not occur for several hours after the initial haemorrhage.

In order to arrest the haemorrhagic tendency rapidly, human fibrinogen should be administered intravenously at the earliest possible opportunity, while of course the blood loss is replaced by adequate blood transfusion. Unfortunately fibrinogen is still in short supply. Multiple transfusions, however, do not supply adequate amounts of fibrinogen, one pint only raising the blood fibrinogen concentration 5–10 mg. per cent. Moore (1954) suggests that at least 2 grammes is necessary and Weiner and his colleagues (1953) advise that 10 grammes of fibrinogen should be kept available as they consider that this amount will be sufficient to treat one patient adequately. Our patient received a total of 435 mg. of fibrinogen. Barnett and Cussen (1954) consider that the amount of fibrinogen required is much less than that advised by Weiner, and their 2 patients received 404 mg. and 390 mg. respectively, which is approximately the same amount as we found necessary. This is a most gratifying finding in view of the small supplies of fibrinogen at present available.

Where fibrinogen is not available fresh blood offers the next best treatment. It must also be remembered that a similar condition of afibrinogenaemia is sometimes associated with intra-uterine death due to Rh incompatability, but it seems only to occur when labour is delayed for many weeks. Amniotic fluid emboli may also

produce an afibrinogenaemia but this condition is fortunately uncommon, so that the combination must be extremely rare.

Although the condition described is relatively rare, it is none the less important that all obstetricians should be aware of this complication of accidental ante-partum haemorrhage, particularly as the diagnosis can be so readily made by the "clot observation" test. Also, although fibrinogen is still scarce, it is now stocked at all the regional headquarters of the Blood Transfusion Service and will be immediately supplied on request.

Summary

A case of severe accidental ante-partum haemorrhage associated with acquired afibrinogenaemia is presented. The aetiology, diagnosis and treatment are discussed. A plea is made for the early recognition of this condition and a mode of treatment is outlined.

Acknowledgments

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VARIATIONS IN PALMAR SWEATING DURING PREGNANCY

BY

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MACKINNON and MacKinnon (1955) observed that the active palmar digital sweat glands in a group of primiparous women, aged 19–25 years, were fewer in the 1st and 3rd trimesters than in the 2nd trimester of pregnancy. However, on statistical investigation this observation was not found to be "significant". The present investigation was made to find if it becomes "significant" when a larger group of women is employed.

METHODS

Two hundred women, 25 in each of the 2nd to 9th months of normal pregnancy, were observed at antenatal clinics in the Middlesex Hospital during the months of January to March in an environmental temperature of 65–72° F. The majority—152—were primiparous, 36 were uniparous, 10 biparous and 2 triparous. Their ages were 20–35 years.

An impression of the skin over the pad of the dried middle finger of the right hand of each woman was made (Sutarman and Thomson, 1952) and the number of active sweat glands in the 4 sq. mm. immediately distal to the central whorl was counted under a magnification of 10. Before making the impressions the women were left seated for half an hour in order to reduce sweating to as near to a basal level as possible, and the procedure was explained to them in the belief that thereby emotional sweat changes would be minimized.

Table I contains the active sweat gland counts in the selected area of skin during the 2nd to 9th months of pregnancy. It also contains the average count in each month, the average count in the 2nd–4th, 5th–7th and 8th–9th months, and pertinent standard deviations.

Fig. 1 presents a graph of the average number of active sweat glands found in the selected area of skin during the successive months of pregnancy.

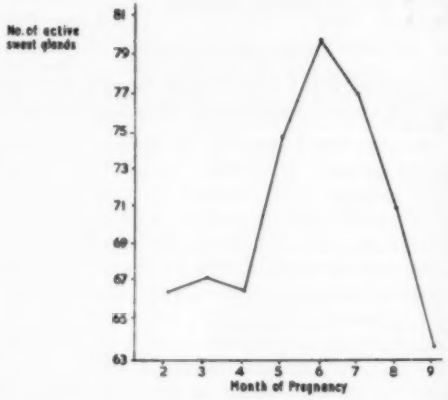

FIG. 1

Graph of the average number of active sweat glands in a selected area of skin during the successive months of pregnancy.

RESULTS

Table I shows that the number of active sweat glands in the selected area of skin varied in the subjects of the present investigation from a minimum of 9 to a maximum of 126. The average was calculated to be 70.

Fig. 1 shows that the monthly average varied from a minimum of 63·6 during the 9th month

TABLE I

The Number of Active Sweat Glands in 4 sq. mm. of Skin Immediately Distal to the Central Whorl of the Right Middle Finger During the 2nd to 9th Month of Pregnancy

	Month of Pregnancy							
	2nd	3rd	4th	5th	6th	7th	8th	9th
	76	74	109	89	83	97	66	66
	57	63	100	85	105	91	66	113
	21	31	82	93	89	43	72	63
	53	84	36	94	82	99	82	62
	32	49	83	43	90	87	57	70
	42	58	61	55	72	71	118	59
	49	111	101	72	118	81	63	59
	32	101	31	46	45	95	114	45
	70	61	109	87	43	70	33	58
	57	71	37	85	123	101	88	23
	41	56	65	75	96	99	70	64
	46	81	37	44	50	96	83	30
	50	49	54	119	47	71	61	43
	98	85	65	111	87	52	73	68
	94	74	30	54	113	80	107	86
	68	55	92	47	53	40	102	72
	124	81	89	38	77	106	25	66
	85	109	74	83	75	85	65	70
	100	62	107	9	105	105	74	50
	92	65	34	76	44	81	89	38
	59	40	69	84	120	70	65	58
	85	31	36	126	23	63	53	108
	62	68	81	56	36	51	70	114
	102	31	64	115	96	60	40	48
	70	93	21	75	124	28	34	59
Average per month	66·7	67·3	66·7	74·4	79·8	76·9	70·8	63·6
Average per group of months ..		66·9			77		67·2	
S.D.		26·1			28·4		25·9	

to a maximum of 79·8 during the 6th month. In addition it shows that the average counts in the 2nd–4th and 8th–9th months were approximately 70 or less; while the average counts in the 5th–7th months were over 70.

Statistical comparison of the average counts in the 5th–7th and 2nd–4th months shows that they differ "significantly", their actual difference being 10 and the standard error of the difference between them 4·45 (Hill, 1950); and statistical comparison of the average counts in the 5th–7th and 8th–9th months shows that they also differ "significantly", their actual difference being 10 with a standard error of 4·9.

Therefore the sweat gland counts obtained during the present investigation were "significantly" lower in the 2nd–4th and 8th–9th months than in the 5th–7th months of pregnancy.

DISCUSSION

The principal known variables which might be called upon to account for the suppression in palmar digital sweating which has presently been demonstrated to take place in the early and late phases of pregnancy are the reproductive hormones—oestrogen, progesterone and chorionic gonadotrophin, and, if any of these is responsible, the graph of its variations during the successive months of pregnancy should resemble directly or inversely the graph in Fig. 1. Oestrogens and pregnanediol gradually increase in amount from the early stages of pregnancy

until near its termination (Cohen, Marrian and Watson, 1935; Browne, Henry and Venning, 1937), and urinary gonadotrophin is maximal in the 2nd month (Browne, Henry and Venning, 1938). Therefore no resemblance exists and it is unlikely that the reproductive hormones are responsible for the differences in palmar sweating at different times in pregnancy.

Suppression of palmar digital sweating was demonstrated by MacKinnon (1954) in the luteal phase of the menstrual cycle, and attributed to increased suprarenal cortical activity. Subsequently the average palmar digital sweating in pregnancy was shown to be still further diminished (MacKinnon and MacKinnon, 1955) and the phenomenon attributed to a further increase in suprarenal cortical activity. Venning (1946) noted not only that urinary corticoids are increased in pregnancy but that they are increased maximally in its early and late stages. thus providing presumptive evidence that suprarenal cortical activity is maximal early and late in pregnancy. It is therefore suggested that increased suprarenal cortical activity was responsible for the active palmar digital sweat gland counts being lower in the 2nd–4th and 8th–9th months than in the 5th–7th months of pregnancy in the women of the present investigation.

Summary

(1) The number of active sweat glands in a selected area of palmar digital skin was counted in 200 resting pregnant women.

(2) The counts were "significantly" lower during the 2nd–4th and 8th–9th months than during the 5th–7th months of pregnancy.

(3) It is postulated that the suppression of palmar digital sweating in the early and late phases of pregnancy was a reflection of increased suprarenal cortical activity.

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FIG. 3
Probe containing four tokographs.

INTRA-UTERINE MEASUREMENT OF PRESSURE DURING LABOUR

Sources of Error

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AN electronic method for intra-uterine measurements of pressure was published in a previous paper (Ingelman-Sundberg, Lindgren and Ljungström, 1953). Large variations of pressure were found between the foetal head and the lower uterine segment. This finding necessitated a special investigation into the sources of error in registration of pressure between the foetal membranes and the uterine wall and between different parts of the foetus and the uterine wall.

The receptors used contained a spring member lying on two edges. The deformation of the member gave a corresponding lengthening of the cemented resistance strain gauges. The variation of resistance was registered electronically in a special AC bridge.

When the receptor was loaded from point to point with weights it had different sensitivity in different parts of the spring member as demonstrated in Figure 1. Calibration in gas or fluid, used in our experiments, corresponds to a pressure uniformly distributed over the spring member. When a receptor, calibrated in this way, is used between the foetal head and the uterine wall with the spring member against the head, the pressure is located on a very limited part of the spring member due to the convexity of the head. In this way a pressure up to twice the real one may be recorded. On the other hand, if the receptor is turned with the spring member against the concave uterine wall the pressure is located near the edges of the receptor, and too low values of pressure are registered (Fig. 8).

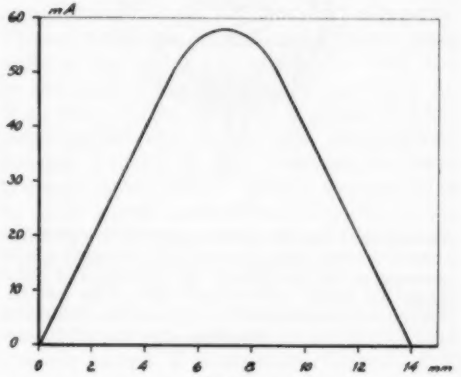

FIG. 1

Strain gauge receptor. Deflections registered when the spring member is loaded with 200 g. at different points along its midline from one edge to the other.

A new receptor was therefore constructed. The spring member is enclosed in a circular metal chamber with an external diameter of 1·8 cm. A circular pellet reaching the surface of the chamber is cemented in the middle of the spring member. The diameter of the pellet is 0·5 cm. The upper surface of the chamber has a convex curvature with a radius of 5 cm. The lower surface has a concave curvature, the radius

being 4 cm. (Fig. 2). The gauge is enclosed in a latex tube, and a probe contains one to four gauges mounted on a spring (Fig. 3). These intra-uterine tokographs give the same calibration curve in air or fluid as when loaded with weights (Fig. 4).

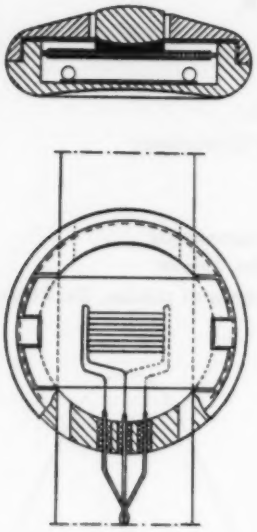

FIG. 2

Intra-uterine tokograph. A spring member is enclosed in a metal capsule with a circular hole containing a pellet cemented at the midpoint of the member. Two strain gauges are pasted one on each side of the member. (See text.) (Manufactured by T. Ljungström, Sollentuna, Sweden.)

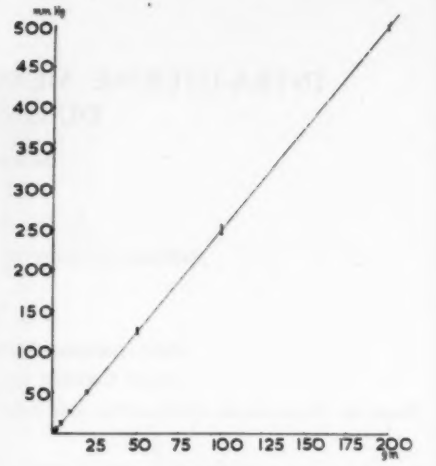

FIG. 4

Intra-uterine tokograph. Relation between measurements in air and loading with weights.

FIG. 5

Strain gauge receptor enclosed in a perforated metal capsule.

In order to know what kind of pressure will be recorded between the foetal membranes and the uterine wall, it is necessary to examine if there is any fluid in the space around the probe. To solve this problem, a strain gauge receptor was surrounded with a perforated metal capsule (Fig. 5) and placed between the foetal membranes and the uterine wall in the uterine corpus of a patient in normal labour. The probe also contained two usual receptors turned with the spring member against the foetal membranes. The receptors were calibrated to give the same deflection for a given pressure. Only small deflections were recorded by the incapsulated gauge previous to the rupture of the membranes (Fig. 6). However, a tendency to increasing deflections was demonstrated during the progress of the registration, but the values measured by the other receptors were not reached until after the rupture of the membranes (Fig. 6). The same observation was made in 12 separate cases.

The following conclusion is drawn from the results obtained. As demonstrated in Caesarean section there is normally no free fluid between the foetal membranes and the uterine wall. Some air is introduced on the application of the probe, giving a non-quantitative transfer of the intra-uterine pressure to the incapsulated gauge. Gradually, however, fluid is secreted into the space, but not enough to give a quantitative transfer of the amniotic pressure. After the

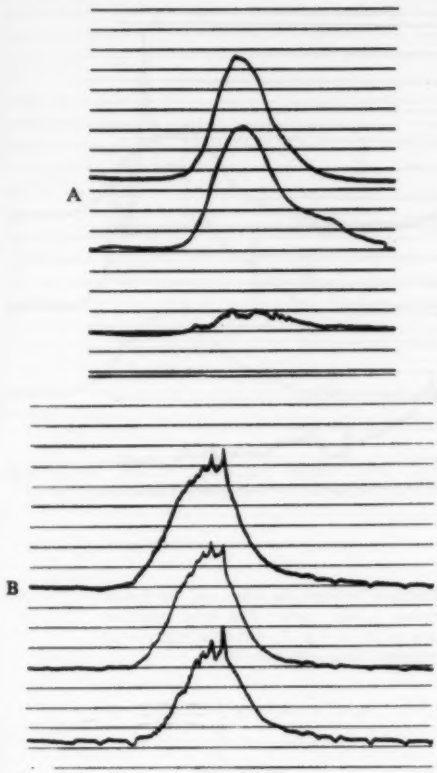

FIG. 6

Pressure curves from receptors applied between the membranes and the uterine wall in the corpus. *Upper curve:* Strain gauge receptor. *Middle curve:* Intra-uterine tokograph. *Lowest curve:* Strain gauge receptor incapsulated according to Fig. 5. A—Before the rupture of the membranes. B—After the rupture of the membranes. Distance between horizontal lines = 10 mm. Hg.

rupture of the membranes, there is fluid enough to fill up the incapsulated receptor and enable quantitative registration of pressure. There is consequently not fluid enough in the space between the foetal membranes and the uterine wall for transfer of the amniotic pressure to the receptor previous to the rupture of the membranes.

When the same experiment was made in the lower uterine segment with the incapsulated receptor between the foetal head and the uterine wall, only small deflections were obtained even after the rupture of the membranes (Fig. 7). In consequence there is either no fluid or only small amounts in this space.

The following experiment was performed in order to demonstrate that the amniotic pressure is recorded by a receptor applied between the intact foetal membranes and the uterine wall. In a patient in normal labour a receptor was placed in the corpus with the spring member against the uterine wall and another one with the member against the foetal membranes. The foetal membranes were punctured in the corpus with a Drew Smythe catheter introduced through the cervix, and the amniotic pressure was recorded according to Williams and Stallworthy (1952). The pressure curve registered by the receptor turned with the member against the foetal membranes is the same as the curve recorded according to Williams and Stallworthy. The curve from the gauge turned with the spring member against the uterine wall is lower, due to the concavity of the uterine wall (Fig. 8). If an intra-uterine tokograph is placed with the pellet against the uterine wall, the amniotic pressure is recorded, but sometimes the curve is superimposed with a pattern corresponding to local muscle contractions (Fig. 9). If the pellet is turned against the foetal membranes, the amniotic pressure is registered.

After the rupture of the membranes, the gauges of both types introduced in the corpus record the amniotic pressure irrespective of how they are turned. It is necessary, however, that sufficient amounts of amniotic fluid be present, as demonstrated by the following experiment.

The amniotic pressure in a patient was recorded according to Williams and Stallworthy and with our method. One receptor was turned with the member against the foetal membranes. After the rupture of the membranes large quantities of amniotic fluid were emptied, and no amniotic pressure could be recorded according to Williams and Stallworthy, but the gauge still registered an irregular curve (Fig. 10). At the Caesarean section which followed only approximately 30 ml. of fluid was left in the uterus, and the gauge was found to be pressed between the uterine wall and the spine of the foetus, thus explaining the irregular curve. In

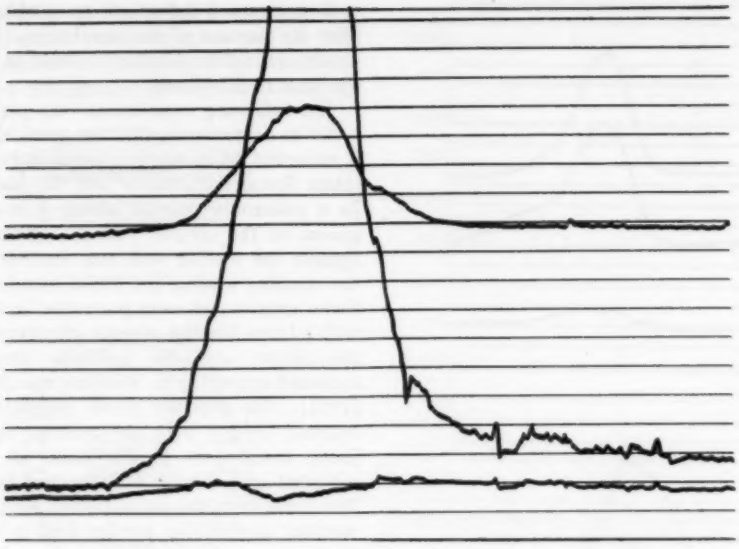

FIG. 7

Upper curve: Amniotic pressure. *Middle curve:* Pressure between the head and the lower uterine segment registered by a strain gauge receptor. *Lowest curve:* The same pressure recorded by a strain gauge receptor incapsulated according to Fig. 5. After the rupture of the membranes. Distance between horizontal lines = 10 mm. Hg.

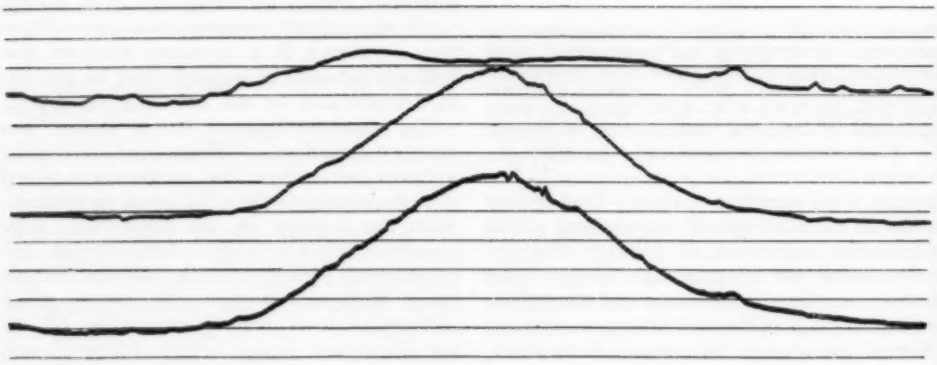

FIG. 8

Upper curve: Strain gauge receptor in the corpus, turned with the member against the uterine wall. *Middle curve:* Same sort of receptor turned against the membranes. *Lowest curve:* Amniotic pressure measured according to Williams and Stallworthy. Distance between horizontal lines = 10 mm. Hg.

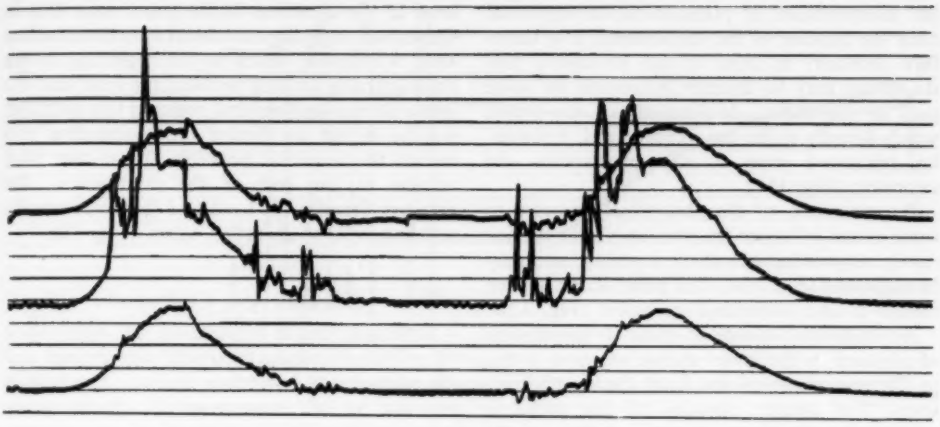

FIG. 9

Upper curve: Amniotic pressure. *Middle curve:* Intra-uterine tokograph turned against the uterine wall. *Lowest curve:* Intra-uterine tokograph turned against the membranes. Distance between horizontal lines = 10 mm. Hg.

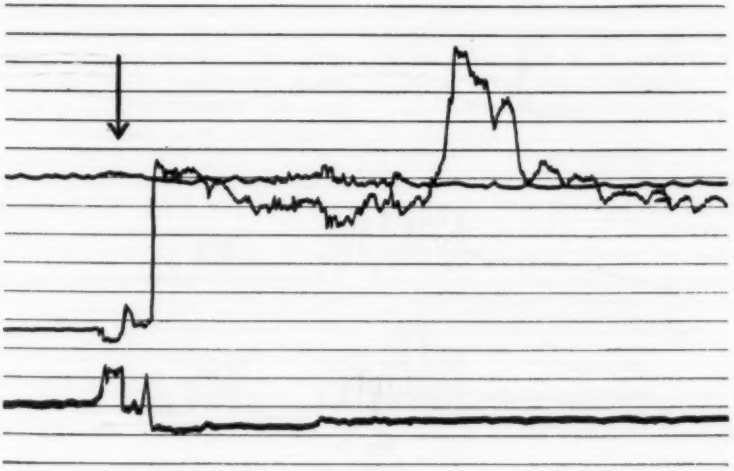

FIG. 10

Upper curve: Strain gauge receptor turned against the uterine wall. *Middle curve:* Strain gauge receptor turned against the foetus. *Lowest curve:* Amniotic pressure measured according to Williams and Stallworthy. The arrow indicates outflow of large amounts of amniotic fluid.

the interpretation of pressure curves registered after the rupture of the membranes, it is therefore necessary to think of the possibility that the gauge may be directly influenced by some part of the foetus. Movements of the foetus which directly strike the receptor will, however, be registered even if the membranes are unbroken (Fig. 11A).

As variations of the abdominal pressure to some extent influence the pressure in the uterine cavity, respiration, coughing, sneezing, etc., may be registered (Fig. 11B). The pulse of the uterine vessels is also sometimes recorded (Fig. 12).

An important source of error in registration of pressure in the lower uterine segment is due to the movement of the head during contractions. The correct position of the probe is controlled by indicators on the shaft, and the probe has very little tendency to slip, as demonstrated by X-ray examination. In the first stage of labour there is only slight movement of the head in the direction of the pelvic axis. But in the second stage the movement may be considerable. A receptor, which at the beginning of the contraction is situated between the head and the lower uterine segment and registers this pressure, will lie higher up during the contraction and record the amniotic pressure. When the head returns at the end of the contraction, the pressure between the head and the lower uterine segment will be recorded again (Fig. 12).

Summary and Conclusion

Different factors influencing the registration of pressure between the foetal membranes and the uterine wall have been studied. The type of receptor is of importance. A strain gauge receptor previously described (Ingelman-Sundberg, Lindgren and Ljungström, 1953) was found suitable only for measurements of the amniotic pressure. For the registration of

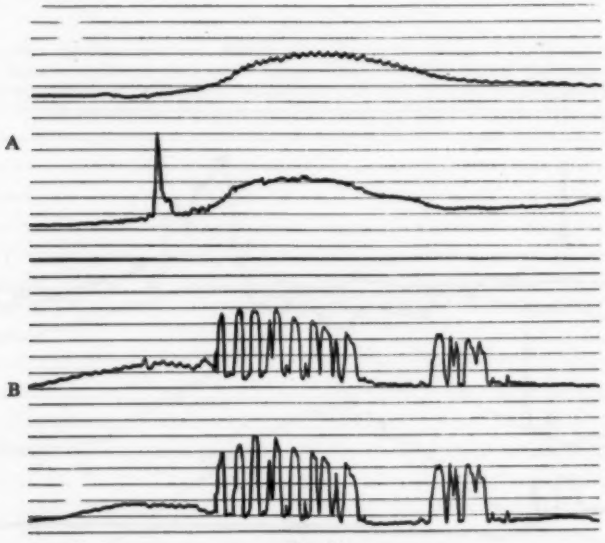

Fig. 11

A—Both curves show the amniotic pressure registered by two strain gauge receptors in the corpus. Small pressure variations due to the respiration are seen, and the spike in the lower curve is due to a foetal movement.

B—The same receptors. The variations of pressure are caused by vomiting.

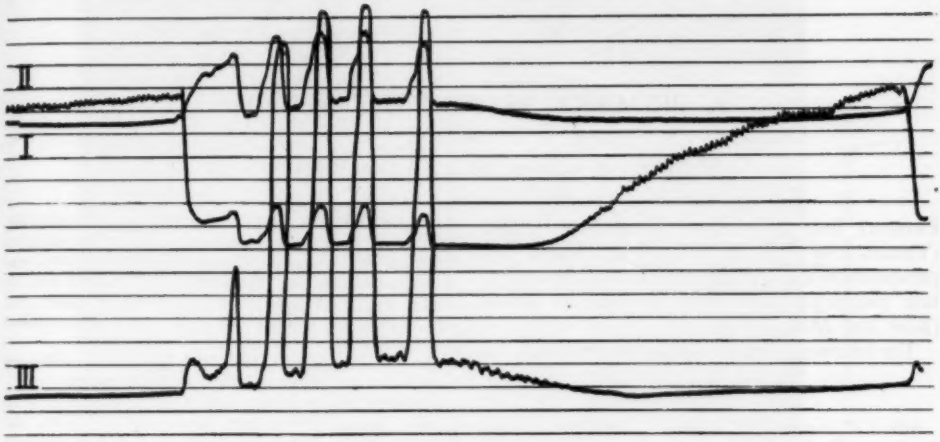

FIG. 12

Curve I. Strain gauge receptor in the corpus. Calibration: Distance between two horizontal lines=50 mm. Hg.
Curve II. Strain gauge receptor in the lower uterine segment. Calibration: Distance between two horizontal lines=100 mm. Hg. The small deflections refer to the pulse of the uterine artery.
Curve III. Strain gauge receptor in the cervix. Calibration=Curve II. For further explanation see text.

local variations of pressure, a new type of receptor has been devised consisting of a small intra-uterine tokograph based upon the strain gauge principle. A receptor sensitive only to fluid pressure cannot be used in the corpus before the rupture of the membranes, as the amount of fluid in the space between the membranes and the uterine wall is not sufficient for the transmission of pressure until after the rupture of the membranes. In the lower uterine segment the amount of fluid is too small even after the rupture of the membranes. For the measurement of the amniotic pressure between the membranes and the uterine wall, it is not possible to use a receptor sensitive to local muscular contractions before the rupture of the membranes. To counteract this source of error the intra-uterine tokograph has to be turned with the sensitive part against the membranes, and in that way the amniotic pressure is measured.

After the rupture of the membranes, a certain minimum of amniotic fluid must remain for the registration of pressure. Movements of the foetus striking the receptors are registered also before the rupture of the membranes and give a characteristic type of deflection.

The correct position of the probe is controlled by indicators on the shaft; it has very little tendency to slip, as demonstrated several times by X-ray examination. By registration of pressure between the head and the uterine wall during the second stage of labour, the movements of the head during contractions cause variations in the pressure registered, as the amniotic pressure is recorded when the head has passed downwards to the receptor.

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A PRIMARY BROW PRESENTATION

BY

H. E. MCNAMARA, M.D., D.Obst.R.C.O.G.

PRIMARY face and brow presentation is rare (Vartan, 1949; Wilkin, 1951; White, 1954). The presentation may vary from time to time during late pregnancy from brow or face to vertex (Kerr and Moir, 1949).

The following case illustrates this feature.

HISTORY

Mrs. C.P., a primigravida, aged 33, had been married for 5 years. Sterility had been voluntary and the first act of coitus in which a contraceptive was not used resulted in the present pregnancy. Her menstrual periods occurred at 25 to 31-day intervals. Her past medical and family history were not relevant.

The last menstrual period was on the 16th October, 1952. The estimated date of delivery was the 23rd July, 1953.

At the 36th week, because of non-engagement of the foetal head, she was referred to the hospital antenatal clinic. Her general medical examination revealed no abnormal findings.

On abdominal examination, the size of the uterus was consistent with 36 weeks of pregnancy. The foetus was in the left occipito-anterior position, and the foetal heart was heard.

Vaginal examination revealed that the promontory of the sacrum was not palpable. The transverse diameter of the outlet was 4 inches (10 cm.) and the subpubic angle was wide.

She attended the antenatal clinic at weekly intervals until she entered hospital on the 18th August, 1953. At each visit the foetal head was above the brim of the pelvis. On the 17th July, 1953, an X-ray pelvimetry revealed a normal gynaecoid pelvis.

The measurements were as follows: True conjugate, 5 inches (12·5 cm.); Bi-spinous, 4·2 inches (10·5 cm); Bi-tuberous, 5 inches (12·5 cm.).

The sacrum was concaved, and the subpubic angle was wide. X-ray examination also revealed an abnormal presentation; there was extension of the cervical spine, and a brow presentation (Fig. 1).

On the 29th July, 1953, X-ray examination showed that there was flexion of the foetal spine, and partial flexion of the head, the position being right occipito-lateral (Fig. 2).

On the 18th August, 1953, when she was 26 days overdue, the patient entered hospital, believing that labour had begun. Her only complaint was backache.

On abdominal examination the foetal head was mobile above the brim. No uterine contractions were palpable. On vaginal examination, the head could not be made to engage. The cervix was soft and taken up, but there was no dilatation. On the 19th August, 1953, there was no change in the physical findings. An X-ray, taken that day, showed the foetus to be in the right mento-lateral position (Fig. 3).

On the 20th August, 1953, the foetal head, although palpable above the brim, was no longer mobile.

History of labour. On the 22nd August, 1953, at 11 a.m. regular uterine contractions began. At 5.50 p.m., the foetal head was engaged in the pelvis. Vaginal examination revealed that the cervix was dilated sufficiently to admit 1 finger, and was well applied to the presenting part.

On the 23rd August, at 12.25 a.m., the patient had an ante-partum haemorrhage, losing 2 ounces of bright red blood. Five minutes later the membranes ruptured spontaneously, and there was no further bleeding.

Apart from this incident, labour progressed satisfactorily and at 4 a.m. the foetal mouth was visible at the vulva.

An episiotomy was performed under local anaesthesia. Subsequent vaginal examination revealed that the chin had not yet descended low enough for spontaneous delivery to occur. Forceps were then applied under pudendal block anaesthesia. At 4.45 a.m. the head was easily delivered, in the mento-anterior position, after a labour lasting 17¾ hours. The child breathed at once. The third stage of labour terminated normally. The puerperium was normal.

The child weighed 6 pounds 13 ounces (3,095 g.) at birth. The right eye and the right side of the face were blue and swollen.

The head was held in the attitude of extension.

Respiratory stridor was present. Twenty-four hours after birth the swelling of the face had almost subsided, but petechial haemorrhages were present.

For six days the attitude of extension persisted. When the normal attitude was assumed, respiratory stridor disappeared (Fig. 4).

Her progress was satisfactory while in hospital and she was discharged, fully breast-fed, on the 14th day of life.

Because the family moved to another part of England, it was not feasible to examine the mother nor baby again, but, when heard from 7 months later, they were in normal health.

DISCUSSION

A primary brow presentation subsequently became a vertex presentation, then reverted to a

FIG. 2
Right occipito-lateral position. 29th July, 1953.

FIG. 1
Brow presentation. 17th July, 1953.

H.E.M.

FIG. 3
Right mento-lateral position. 19th August, 1953

FIG. 4
Child—aged 6 days.

brow presentation and ultimately delivered as a face presentation.

The cause of the malpresentation was not evident, but, in view of the ante-partum haemorrhage which occurred during labour, might have been due to placenta praevia of the first degree.

Increased tone of the extensor muscles of the neck as a cause of primary face and brow presentation has been referred to in the literature (Gibberd, 1939; Vartan, 1949; Wilkin, 1951; White, 1954) and may have been the cause in this case.

Although pregnancy lasted 30 days beyond the estimated date of delivery, the child weighed only 6 pounds and 13 ounces (3,095 g.). The mother had noted her last menstrual date in her diary, and as she was an intelligent woman, I presume that it was correct.

This case is reported by courtesy of Mr. D. J. MacRae and Mr. Stephen Scorer, Obstetricians to the Watford Maternity Hospital, and Dr. M. E. Edmunds, Paediatric Physician to the hospital.

To Mr. D. M. Stern, for his kindly criticism, my thanks are due.

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PREGNANCY AFTER EXTENSIVE MYOMECTOMY

BY

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THIS case is reported for the following reasons:

1. The patient was only 22 years old and she had a very large fibroid.

2. Pregnancy followed 5 years later in a uterus so disturbed that it had appeared 2 months after myomectomy operation that the cervix was separated from the body of the uterus by a fistulous track (Fig. 1).

3. The operation was technically difficult and even dangerous for the patient but that it was worth while has been fully justified subsequently.

Victor Bonney (1946) stated that the youngest patient on whom he performed the operation of myomectomy was 19. He also stated that "numbers plus weight is a more reliable guide, and on this reckoning I am proudest of the patient from whom I removed 40 tumours whose combined weight after removal was 21 pounds. In drawing attention to these exceptional operations I hope I shall be absolved of boastfulness, but it is necessary to relate them in order to show the command surgery has obtained over cases, for which only a very few years ago hysterectomy would have been deemed the only possible means of cure." In Bonney's series of cases 38 per cent conceived after myomectomy operation. Natural delivery ensued 34 times, Caesarean section was performed 17 times, and there was 1 miscarriage. The largest number of tumours removed from a uterus which subsequently became pregnant was 35. In 40 per cent of all Bonney's cases the tumour was single, and in 60 per cent multiple.

Miss L., aged 22, was sent to the Outpatient Department of the Radcliffe Infirmary, Oxford, on 20th February, 1947, by her doctor because she had had menorrhagia of 3-months duration. In fact, she had only had 7 clear days in that time and the continuous loss was interfering with her work. In addition to the complaint of menorrhagia she had had a cramping pain in the right leg at menstruation for 4 months and she stated that she had been putting on weight for 2 months. There were no other complaints.

On examination she was a rather short, stout individual. There was enlargement of the abdomen on inspection but this could have been mistaken for obesity. Further notes recorded at the time were as follows:

"Hardish tumour—symmetrical—arising from pelvis nearly to ensiform cartilage—no thrill—no free fluid." Inspection of the vulva showed that she was *virgo intacta*. Rectal examination was unsatisfactory as the bowel was loaded. There were no breast changes and no foetal parts could be felt. I remember at the time telling the students that it was very much like an ovarian cyst except for its hardness. X-ray of the abdomen was reported on as follows: "Large abdominal tumour arising from the pelvis. There is a group of calcifications above and to the right probably in the lymphatic glands. The tumour shows no distinctive features" (Dr. F. Reid).

The pre-operative diagnosis gave rise to considerable speculation until Bonney (1946) was consulted on the night prior to operation. His statement that the youngest girl he had performed myomectomy on was 19 years of age made more likely the diagnosis of large uterine fibroid.

The operation was undertaken under general anaesthesia on 14th March. A midline sub-umbilical incision was used and it had to be extended to the right at umbilical level. The operative findings were:

1. Enormous "cystic" fibroid arising from the cervical region and extending into the right broad ligament. There was much distortion of uterus most of which was perched on the top of the fibroid.
2. The ovaries were normal.
3. Operative procedure—Blood drip was set up and 2 pints of blood were transfused during the operation which took about 2 hours. The right round ligament was bisected and the incision was extended round to the front of the tumour. The fibroid was enucleated with considerable difficulty without excessive haemorrhage. The difficulty arose because the fibroid was undergoing inflammatory and cystic degenerative changes so that a proper cleavage plane was not obtained. (Indeed, I removed in the first instance most of the fibroid and later the rest of it in a layer about ¼ inch thick which has been described in the pathological report as a cyst and was not included in the

FIG. 1

Hysterosalpingogram two months after operation.

total weight of fibroid removed.) The uterine cavity was opened during enucleation; no other fibroids were seen and the endometrium was stitched with fine catgut as far as it was identifiable. The cavity which was extensive was obliterated with interrupted catgut sutures and the right round ligament was reconstituted. The tubes were tested at the end of the operation and both found to be patent. The wound area was re-peritonealized and the abdomen was closed in layers.

The post-operative convalescence was entirely satisfactory except for a slight weakness of the right hand due to a lesion of the right brachial plexus. Dr. Ritchie Russell described this as "anaesthetic palsy". By 3rd June, 1947 recovery of the hand was complete. The patient was discharged from hospital on the 29th March.

The pathological report (Dr. Robb Smith) was as follows:

"The specimen consisted of a fibroid, $14 \times 15 \times 10$ cm., and weighing 6 kilos. The fibroid was encapsulated and lobulated. There was also a cyst 10×10 cm., the greatest width of the wall being 2 cm. The cyst had been opened and had a roughened epithelium. Microscopic examination of the larger mass showed a fibroid, without remarkable feature. The cyst apparently was a degenerated fibroid." (The cyst was, in fact, the capsule of the fibroid.)

I am greatly indebted to Professor Chassar Moir who showed me this same girl now under a different name (married) in the Radcliffe Infirmary after Caesarean section on the 27th June, 1953. She had had a live child weighing 8 pounds. The following is an extract from the letter sent to her doctor on the 15th July, 1953: "This patient did very well during her pregnancy except that she had marked oedema of her legs and abdominal wall during the latter half, which was only partly controlled by rest and salt restriction. She was admitted to hospital on the 13th June and was then 38-weeks pregnant.

"After a period of rest Caesarean section was carried out on the 27th June. There were multiple adhesions inside the abdomen obliterating the peritoneal cavity in front of the uterus. The anterior wall of the uterus was incised by a classical incision; the baby was a girl, birth weight 8 pounds 2 ounces, and both mother and child made good progress. They were discharged home on the 10th July."

At the Postnatal Clinic on 11th August a note was made that the uterus was bulky and a small fibroid was palpated in the lower part of the uterus on the left side.

I should like to express my sincere thanks to Professor Chassar Moir, and to Dr. Ian Skinner who sent the case to me in the first place. This patient was treated while I was First Assistant in the Nuffield Department of Obstetrics and Gynaecology, Oxford.

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ACUTE MONOCYTIC LEUKAEMIA IN PREGNANCY

BY

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ALTHOUGH more than 100 cases of leukaemia associated with pregnancy have been reported, it is of interest to note that only 4 of these have concerned acute monocytic leukaemia. I wish to record here a fifth case and to present a comparative summary of the main findings recorded in these 5 cases.

CASE REPORT

Mrs. C.D., aged 31 years, was admitted on 19th July, 1948, to Stobhill Hospital, Glasgow. She had had 5 previous pregnancies all resulting in live normal children. Her last menstrual period was on 3rd January, 1948 so that her expected date of confinement was 10th October, 1948. Except for spinal tuberculosis, for which she received treatment in a sanatorium from 1936 to 1938, her past medical history was not remarkable. Her antepartum record during this pregnancy showed that she had attended a City Corporation clinic from 10th March and that her only complaints had been weakness and tiredness. The pelvis was adequate in size, Kahn test negative, urine normal, blood group O IV, Rh positive.

On 20th June she complained of toothache and, visiting her dentist, was told that all her upper teeth were carious and loose; there had never been any bleeding from the gums. Under local anaesthesia he extracted all her upper teeth apparently without difficulty. That evening she had a brisk haemorrhage from the sockets but it ceased spontaneously after 4 hours. On the following day she observed that the slightest knock or injury to the skin was sufficient to cause a large bruise, and by that evening there were 10 or 12 such ecchymoses of varying size visible on both arms and legs. During the next 4 weeks, bruises of this type continued to appear and, although able to carry out her household duties, she felt increasingly weak and breathless. During the night of 19th July she rose from bed to pass urine and found it coming away "like pure blood". She also complained of severe frontal headache and vomited 3 times, the vomited material being brown in colour.

Examination on admission revealed a pale, tired-looking woman with a tinge of sclerotic jaundice. Her temperature was 98·4 degrees Fahrenheit, the pulse rate 118 per minute and the respiration rate 18 per minute. About 40 ecchymoses varying in size from 5 to 30 millimetres were irregularly distributed over both arms, both legs and buttocks. A slight degree of kyphosis was present at the site of her old spinal tuberculosis. There was no enlargement of the superficial lymph glands. She had marked halitosis and her upper gums, though pale and slightly swollen, were satisfactorily healed. The lower teeth were carious and there was marked gum retraction, but the gums were not spongy though the papillae were proliferated and chronic gingivitis was present. The tongue papillae were normal. Enlargement of the uterus to the size of a 26-weeks pregnancy was noted, the foetus lying longitudinally in the left occipito-anterior position. The foetal heart was heard below and to the left of the umbilicus. The liver and spleen were enlarged and tender and extended 10 and 6 centimetres below the right and left costal margins respectively. There was no ascites. On ophthalmoscopic examination both fundi appeared normal. A catheter specimen of urine was port-wine coloured. The specific gravity was 1,035 and the reaction acid. Albumen was present, the Esbach reading being 2 grammes per litre and this was considered to be more than could be accounted for by the presence of blood alone. Urobilin was present in small amount but no bile, sugar or ketones. Microscopic examination of the urine showed numerous red blood cells, white blood cells and a few urate crystals.

Her haemoglobin was 34 per cent (Sahli) and red blood cells were 1,580,000 per c.mm. with 13 per cent reticulocytes. White blood cells were 24,500 per c.mm. with 8·4 per cent neutrophil polymorphs, 5·2 per cent small lymphocytes, 7·2 per cent large lymphocytes, 63·6 per cent stem cells, 2 per cent myeloblasts, 4 per cent myelocytes, 2·4 per cent premyelocytes, 4·2 per cent monocytes, 0·8 per cent erythroblasts and 2·2 per cent normoblasts. The predominant leucocyte was the stem cell, 16–20 μ in diameter with a large, folded, segmented oval or reniform nucleus and a thin surrounding band of greyish-blue cytoplasm (Fig. 1). The cell boundary was often irregular due to the extension of pseudopodial processes as described by Levine (1934). Nucleoli were scanty and indistinct. These cells showed a moderate positive reaction on oxidase staining. Platelets were 35,000 per c.mm., bleeding time 20 minutes, coagulation time 5 minutes (clot retraction very poor) and prothrombin time 80 seconds for plasma and 130 seconds for plasma diluted 1 in 10. Examination of sternal marrow revealed marked hyperplasia and stem cell infiltration; normoblastic blood regeneration was evident and there was proliferation of monoblasts but no striking excess of myeloblasts.

1 Pl.

The blood urea was 28 mg. per 100 ml., the blood cholesterol 190 mg. per 100 ml., the serum proteins 6·98 g. per 100 ml. (albumen 4·40 g.—globulin 2·58 g.), the alkaline phosphates 8·7 units per 100 ml., the plasma chlorides 479 mg. per 100 ml., the serum bilirubin 0·3 mg. per 100 ml., the plasma ascorbic acid 1·6 mg. per litre and the blood sugar 120 mg. per 100 ml. The Paul Bunnell reaction for infectious mononucleosis was negative and 3 blood cultures were negative. Radiograms of chest and abdomen were normal.

It was concluded that the case was one of acute monocytic leukaemia of Naegeli type.

Treatment

Two pints of matched whole blood were administered with considerable general improvement in her condition. Courses of penicillin and sulphadiazine were commenced along with calcium lactate, vitamin K, vitamin C, crude liver extract and glycothymoline mouth washes. She was given a light diet rich in protein. Deep X-ray therapy was not undertaken in view of her poor general condition and possible harmful effect on the foetus.

Progress

During the next few days her general condition deteriorated rapidly and a low grade diurnal fever developed.

On 25th July she was given another transfusion of 2 pints of whole blood. On 27th July she reported the cessation of foetal movement, and on auscultation no foetal heart sounds could be heard. Her temperature rose to 103·2 degrees Fahrenheit, pulse rate to 118 per minute and respiration rate to 24 per minute. Her face had become flushed and swollen and she complained of acute pain in the left hypochondrium; she vomited 3 times and on each occasion the vomitus contained a small amount of altered blood. The spleen was now palpable 10 centimetres below the costal margin and was acutely tender. The lower gums were now dark in colour, necrotic and foul smelling. On 29th July multiple petechial haemorrhages appeared on the palms of the hands and on the anterior abdominal wall and many new ecchymoses were noted on the arms and legs. The haemoglobin was now 38 per cent (Sahli) and the red blood cells were 1,400,000 per c.mm. with 2 per cent reticulocytes. White blood cells were 98,000 per c.mm. with 1 per cent neutrophil polymorphs, 2 per cent small lymphocytes, 8 per cent large lymphocytes, 68 per cent stem cells, 2 per cent myeloblasts, 6 per cent myelocytes, 6 per cent premyelocytes, 4 per cent monocytes, 1 per cent erythroblasts and 2 per cent normoblasts.

On the following day at 1 p.m. uterine contractions commenced and a further transfusion was set up in case of severe uterine haemorrhage. After 5 hours of uneventful labour, delivery of a macerated infant occurred spontaneously. Separation of the placenta took place 5 minutes later and it was expressed from the vagina without difficulty; the total amount of blood lost during parturition was estimated at about 3 ounces.

One hour after delivery she became restless and perspired freely. After 3 minutes of violent convulsions she lapsed into a deep coma and during the next 3 hours her temperature rose steadily to 106 degrees Fahrenheit. She died at 5 p.m. without recovering consciousness.

Pathologist's Report

Infant. Autopsy performed 2 hours after delivery. Length, 41 centimetres. Weight, 1·165 kilogrammes. Death had probably occurred some days previously as there was gross desquamation of epithelium.

Section and naked eye examination of liver, spleen, bone marrow, lungs, thymus, heart, kidneys, pancreas and adrenals revealed no evidence of leukaemic infiltration and no other abnormality. There was no enlargement of lymph nodes.

Histology of these organs and of bone marrow was valueless as all were partially autolyzed and necrotic.

Placenta. This measured 15 centimetres in diameter and weighed 240 grammes. Multiple greyish pink homogeneous infarcts were noted, the largest measuring 2 centimetres in diameter. It was in a fairly good state of preservation and on histological examination the cell characters could be clearly distinguished. In the intervillous blood spaces vast numbers of leucocytes were present and in places were grouped together forming thrombi composed almost entirely of white blood cells. By contrast, the tissue of the villi was normal and showed no evidence of leucocytic infiltration.

Mother. Autopsy performed 17 hours after death.

External Examination. Numerous haemorrhages and petechiae were seen over the skin of the entire body. The superficial lymph nodes were not enlarged. The gums were hypertrophied with patches of ulceration and necrosis and a blood-stained froth filled the oral and nasal passages.

Internal Examination. Blood stained fluid was present in the right and left pleural spaces, in the pericardium and in the peritoneal cavity. The serous surfaces of the body cavities presented numerous petechial haemorrhages.

The lower lobes of both lungs were red in colour and were completely consolidated. Numerous petechial haemorrhages were noted on the mucous surface of stomach, small intestine and large intestine. The liver was

grossly enlarged and weighed 2,965 grammes; it was pale in colour and mottled. The spleen weighed 1,365 grammes, was enlarged to about 6 times the average size and contained numerous infarcts, some pale in colour and others red. The lymph nodes along the abdominal aorta were enlarged and haemorrhagic and a few enlarged lymph nodes were located alongside the iliac vessels; there was no gross enlargement of any other lymph nodes in the body. The tonsils were normal.

The kidneys were greatly enlarged and were firm in consistency. Throughout both kidneys, numerous small haemorrhages had occurred and, in places, had become confluent forming large haemorrhagic zones. The remainder of the kidney substance was pale in colour. A small amount of blood-stained urine was present in the urinary bladder and a few petechial haemorrhages were noted in the lining of this viscus.

The uterus, cervix, vagina, ovaries and Fallopian tubes showed no gross change other than that found immediately following parturition.

There was considerable enlargement of the thyroid gland and numerous small haemorrhagic cysts were present in the lower pole of each lobe.

The cerebral convolutions were markedly flattened. A large haemorrhage had occurred into the internal capsule of the left cerebral hemisphere. No haemorrhage was seen in the midbrain or pons but numerous small haemorrhages varying in diameter from 2 to 5 millimetres were present throughout the cerebellum.

Histology. Microscopic examination of the prepared sections showed extensive leukaemic infiltration of the lungs, heart, liver, spleen, gastro-intestinal tract and kidneys, adrenals, uterus, ovaries, Fallopian tubes, bone marrow, gingivae, cerebellum, both cerebral hemispheres and lymph nodes (taken from the groups of enlarged nodes along the aorta and iliac vessels).

Pathologist's Comment. The case was one of acute leukaemia occurring in a woman 7-months advanced in pregnancy. The cerebral haemorrhage occurred merely as a terminal incident.

Discussion

The first case of monocytic leukaemia complicating pregnancy was described by Williams (1948). A year later Birge, Jenks and Davis (1949) reported a case in which the patient, a 38-year-old woman, was admitted to hospital during the 7th month of pregnancy with symptoms of eclampsia and found to have the characteristic blood picture of acute monocytic leukaemia. Delivery of a non-viable infant coincided with the onset of complete remission of the leukaemia for 21 months but recurrence of the disease culminated in death 2 months later. First and Wellenbach (1951) and Beven (1951) described further cases, the latter being complicated by pulmonary tuberculosis.

The total number of cases reported is thus 5 and several common factors emerge from a study of these records. In all 5 cases, the onset of leukaemia was recognized during the 7th month of pregnancy and in each instance the disease, with or without remission, followed an irregularly febrile course culminating in the death of the mother. Skin petechiae appeared in all cases, but lymph gland enlargement, splenomegaly and hepatomegaly were not constant findings. There was involvement of gingivae in all cases except that of Birge *et al.* (1949). Severe anaemia accompanied the disease in every case but the degree of leucocytosis showed considerable variation and failed to give a satisfactory indication of the severity of the disease. Serious haemorrhage during or after the confinement did not occur in any of the reported cases.

In no case was the infant found to be leukaemic and further proof that the placenta presents a barrier to the disease was given by histological examination of that organ in the cases of Birge *et al.*, First and Wellenbach, and Barr where leukaemic cells were found in the intervillous spaces but not in the chorionic villi.

At necropsy of the mother, leukaemic infiltration of liver, spleen and lymph nodes was noted in all 5 cases. In 3 cases there was infiltration of all organs but in the case of Birge *et al.* the only other tissue involved was bone marrow and, in the case of Beven, the only other tissues involved were the lungs and the left eye where there was a small sub-retinal deposit.

With regard to treatment, blood transfusion and antibiotic therapy were employed in all cases. Radioactive phosphorus, used by Birge and his co-workers produced a reduction in

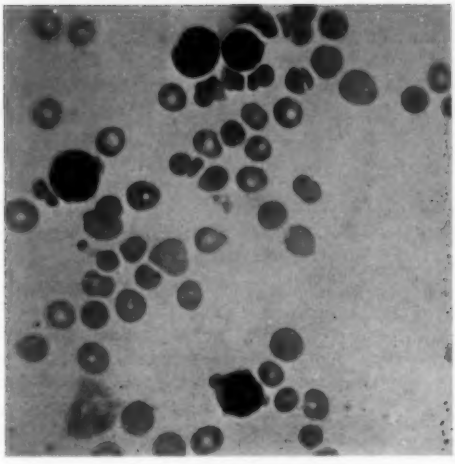

FIG. 1

Showing the large stem cells. The pseudopodia can be seen in the cell at the bottom of the picture. Marked anisocytosis and poikilocytosis of the red cells is evident. ×850.

leucocytic and thrombocytic counts but no clinical improvement. First and Wellenbach reported no response from the use of nitrogen mustard and Beven found urethane equally ineffective. Harris (1953) in reviewing the literature on leukaemia and pregnancy states that A.C.T.H., cortisone and aminopterin (4-Aminopteroyl Glutamic acid) are of no value in treatment although the latter substance was employed with some success by Farber and his co-workers (1948) in the treatment of 16 children suffering from acute leukaemia.

Haines (1941) reported no success with the neo-prontosil (disodium 4-sulfamido-phenyl-2-azo-7-acetyl-amino-1-hydroxy-naphthalene, 3, 6-disulfonate).

Until a cure for leukaemia is obtained it would seem that the management of this distressing complication of pregnancy is restricted to correction, so far as it is possible, of the concomitant anaemia and the prevention of septic complications. Deep X-ray therapy is of little value in acute leukaemia and carries with it the added risk of damaging a foetus which seems to be protected by the placenta from the leukaemic process.

Summary

(1) A case of acute monocytic leukaemia complicating pregnancy is presented.

Delivery of a stillborn child was followed 4 hours later by death of the mother from cerebral haemorrhage. The infant was not affected by leukaemia.

(2) A short review of the literature, 5 cases in all, is presented and the findings commented upon.

(3) There is no specific treatment for leukaemia and the management of such cases is directed towards treatment of the anaemia and prevention of septic complications.

Acknowledgment

The late Dr. Adam Barr granted permission for the publication of this case record of one of his patients.

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ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

THE following were admitted to the Honorary Fellowship of the College on Friday, 22nd July, 1955:

His Excellency, The Governor General of Canada, The Rt. Hon. Vincent Massey, P.C., C.H.

Dr. George Corner of Baltimore, U.S.A.

A MEETING of the Council was held in the College House on Saturday, 23rd July, 1955, with the President, Sir Arthur Gemmell, in the Chair.

Charles David Read, Esq., M.B., Ch.B., F.R.C.S., F.R.C.O.G., was elected President and will assume office in October.

Andrew Moynihan Claye, Esq., M.D., F.R.C.S., F.R.C.O.G., and Victor John Frederick Lack, Esq., M.B., B.S., F.R.C.P., F.R.C.S.E., F.R.C.O.G., were elected Vice-Presidents.

The following officers were re-elected:

Honorary Treasurer
Arthur Capel Herbert Bell, Esq., M.B., B.S., F.R.C.S., F.R.C.O.G.

Honorary Librarian
Arthur James McNair, Esq., M.A., M.B., B.Ch., F.R.C.S., F.R.C.O.G.

Honorary Secretary
Ian MacGilchrist Jackson, Esq., M.B., B.Ch., F.R.C.S., F.R.C.O.G.

Honorary Curator of the Museum
Richard Alan Brews, Esq., M.D., F.R.C.S., F.R.C.O.G.

Honorary Treasurer, Australian Regional Council
John Chesterman, Esq., F.R.C.S.E., F.R.C.O.G.

Honorary Treasurer, New Zealand Regional Council
James Edmett Giesen, Esq., M.D., B.S., F.R.A.C.S., M.R.C.O.G.

The following officer was elected:

Honorary Treasurer, Canadian Regional Council
George Albert Simpson, Esq., M.D., F.A.C.S., F.R.C.O.G.

The following were appointed Sims-Black Professors for 1956:

Andrew Moynihan Claye, Esq., M.D., F.R.C.S., F.R.C.O.G.
and
Charles Horner Greer Macafee, Esq., F.R.C.S., F.R.C.S.I., F.R.C.O.G.

The following were elected to the Membership of the College:

Hugh McKinven Goldie Agnew.
Max Michael Baskin.
Lokenath Bhose.
Max Leonard Bloom.
Alec Graeme Bond.
Edward Patrick Campbell.
Tuck Kwong Chong.
Mary Gertrude Coyle.
John William Gwynne Evans.
Ralph William Forman.
Meenakshi Ghosh.
John Angelo Holmes.
Laurence Maurice Jacks.
John Donald Campbell Lyons.
John MacVicar.
Nirupama P. Nayak.
Mary Phillips.
Israel Rocker.
Jacobus Petrus Roux.
Alan H. Rowson.
Samuel Sacks.
John Rudolf Saunders.
Muriel June Scudamore.
Herbert Gerald Irwin Shanks.
Colin Douglas Smith.
Robert McNeill Thomson.
Robert Fife Zacharin.

REPORTS OF SOCIETIES

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

FEBRUARY 1955

A Meeting of the North of England Obstetrical and Gynaecological Society was held in Liverpool on Friday, 18th February, 1955.

Mr. J. B. Cochrane reported a case of

LACTATING ADENOMA OF THE BREAST

Mr. Cochrane wished to bring this case to the notice of the Society in order to illustrate the difficulty it presented in diagnosis.

The patient was first seen by Mr. Cochrane when she was 10-weeks pregnant, and at that initial visit no abnormality was noticed. When she visited the clinic 2 weeks before term she stated she had noticed a lump in the right breast on the previous day, and it was recorded as a nodular induration just outwith the lateral boundary of the areola.

One week later Mr. Cochrane saw the patient himself and found a tumour the size of a plum, hard, circumscribed and freely mobile over deep tissues. No axillary glands were felt and it was decided to wait a further week, when the condition was again found materially as before. The patient was now at term and she was admitted and the opinion of a surgeon sought. Aspiration produced only a few drops of blood. It was then thought prudent to effect delivery and following surgical induction of labour spontaneous delivery occurred.

The next day the lump in the breast was reviewed and the possibility of a carcinoma was strong. In view of the rapid growth and dissemination of such a neoplasm in the lactation period it was decided to resort to surgery. One week after delivery the breast was explored, and the tumour found to be a rounded encephaloid mass some 3 inches in diameter, not well circumscribed nor apparently encapsulated. It was felt that the clinical presumption of carcinoma was confirmed and radical amputation was performed. There was no evidence of gland involvement at the time of operation.

Microscopic examination of the tumour gave rise to doubt as to its true identity and it was referred for further opinion. It was agreed that the tumour was not a carcinoma but a lactating adenoma.

When the breast tissue was fixed, the tumour appeared quite well defined, apparently encapsulated, reduced in size, and altogether not at all like its appearance *in situ*.

Microscopy showed an adenoma composed of closely packed functional glandular lobules, which had undergone rapid expansion in response to the stimulus of lactation—a lactating adenoma. The glandular acini were collected into well defined lobules with no evidence of fibrous tissue proliferation.

Mr. Cochrane had been unable to find reference to the potential and actual rapid alterations these benign tumours may undergo in pregnancy and lactation, nor any guidance about the possible clinical confusion of these rapidly enlarging tumours and frank carcinoma.

Dr. J. K. Wilson read a short paper on

INVESTIGATION OF PLACENTAL SEPARATION BY CORD INJECTION

Mr. Trevor Johnson gave a preliminary report on

STUDIES IN PLACENTAL ACTION DURING PROLONGED AND DYSFUNCTIONAL LABOURS USING RADIOACTIVE SODIUM

(This article appears on page 513 of this issue)

Discussion

Dr. T. A. Chalmers stated that Flexner had published a curve showing that placental transfer of sodium depended on the period of gestation, and had this been found?

Mr. P. Malpas said that there was a great deal mentioned about placental insufficiency, forgetting that it was the foetus that pushed the blood through the placenta. He thought that in some cases the insufficiency was foetal and not placental.

Professor Jeffcoate said that when Cox and Chalmers were working on this problem, the question of sodium restriction in the toxaemias of pregnancy affected the issue. He asked if this difficulty had been met and how it had been overcome.

Mr. Johnson and Mr. Clayton in their reply stated that all the patients had been delivered at term, and cases of pre-eclampsia had been avoided. They were purely drawing a comparison between what the mother was given and what the baby received.

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

MARCH 1955

A Meeting of the North of England Obstetrical and Gynaecological Society was held in Sheffield on 18th March, 1955.

Mr. C. J. Dewhurst described

A CASE OF ORAL AND VULVAL ULCERATION WITH INFLAMMATION IN THE EYE

(This article appears on page 562 of this issue)

Discussion

Dr. Ian Sneddon discussed the condition from the dermatologist's point of view. He said that aphthous ulcers of the mouth were relatively common. Many were severe, painful and disabling. Some 3 cases in every 100

had associated vulval ulceration. A careful investigation had not disclosed any common aetiological factor. There were two conditions to be considered in differential diagnosis:

(1) Erythema multiforme which sometimes involves the mouth and vulva. The mucosa becomes sodden and ulcerated, but the ulcers were not very painful. The process was essentially an acute one and healing occurred in 2 to 3 weeks.
(2) Ocular and benign mucous membrane pemphigus. The primary lesion in this condition was a vesicle and associated with oral ulceration there was often severe eye involvement.

The President, Mr. Malkin, drew attention to the frequency of the condition in Eastern Mediterranean countries.

Mr. Herd felt that there was some association between the condition described and achlorhydria and anaemia. Treatment of the latter condition would lead slowly to improvement and cure.

Professor Russell spoke of the value of an interchange of ideas between specialists in solving problems of this nature. He wondered what fuller investigations might be done to discover the cause of the condition.

In reply to the discussion Dr. Sneddon drew attention to the fact that aureomycin was effective even after heating which would probably destroy any antibiotic effect.

Mr. P. C. Steptoe reported

A Case of Cancer of the Colon and Ovary Complicating Pregnancy

Mr. Steptoe said that cancer of the colon complicating pregnancy was not a common lesion, though he hesitated to call it rare. Banner, Hunt and Dixon reviewed the literature in 1945 and found 62 case reports in the past 70 years, in which the maternal mortality was 63 per cent and the infant loss 50 per cent. The writers added a further 7 cases with maternal mortality of 14 per cent and infant mortality of 28 per cent. Three further cases have been reported since then by Bacon and Rowe (1947), Waters and Fenimore (1954) and Schuyler (1955), bringing the total including Mr. Steptoe's case to 73. Mr. Steptoe found from perusal of the literature that the high maternal mortality was associated with misdiagnosis of the lesion until its late manifestations.

Mr. Steptoe summarized a few facts about the malignant colon complicating pregnancy:

(1) The average age of the patients was 32.
(2) The descending colon was the commonest site.
(3) Loss of weight was not usual.
(4) Mild secondary anaemia was invariably present.
(5) The commonest symptoms were constipation, diarrhoea, abdominal cramp, nausea and vomiting and bloody mucinous stools.

Waters and Fenimore in their review suggest that X-rays may be misguiding in the last half of pregnancy.

Case Record

Mrs. A.C., a primigravida, aged 30, was seen at hospital first on 25th June, 1954, when 34-weeks pregnant. There was a long history of constipation which had been present approximately 12 months before the onset of pregnancy. It had been associated with occasional attacks of colicky pain in the left iliac fossa which had been treated with diet and antispasmodic drugs. Apart from increasing constipation and attacks of pain in the left iliac fossa she had been well, but these symptoms had been worse in the last few days.

Mr. Steptoe found the patient to have a pale, toxic appearance, a furred tongue and offensive breath. On abdominal examination the uterus was consistent in size with a single pregnancy of 34-weeks duration and displaced slightly to the right. There was marked flatulent distension of the abdomen so that the bowel was lying in front of the uterus, occupying the whole of the upper and left lower abdomen. On deep palpation to the left of the uterus there was a vague sensation of resistance and dullness to percussion, elsewhere being tympanitic. Rectal and vaginal examinations revealed nothing abnormal.

The patient was admitted to hospital and was treated with enemata and suppositories with some improvement. At this time she showed mild anaemia, there was no vomiting and the stools though constipated were normal. When 35½-weeks pregnant the constipation became more severe, later she became dehydrated and intravenous fluids were given. Mr. Steptoe then decided to induce labour by rupture of the membranes, and after 9 hours in labour a living infant weighing 5 pounds 8 ounces was delivered. The mother's general condition improved following delivery, but as some dehydration was still apparent the transfusion was continued. On the third post-partum day there was a rise in temperature and pulse rate, her condition deteriorated and it was decided to perform a caecostomy and explore the abdomen.

A caecostomy was done and drained freely through a Paul's tube. As the patient's condition improved a general anaesthetic was then given and an exploratory laparotomy performed. A large semi-solid tumour which appeared to be completely encapsulated was found arising from the left ovary. It was lying across the left side of the transverse colon, which was grossly distended proximal to it. The uterus and right ovary appeared normal, and the tumour only when resected revealed a typical constricting annular carcinoma of the sigmoid colon. Further surgical treatment was not considered wise at this stage and the abdomen was closed.

The patient's condition improved enormously with streptomycin, penicillin and intravenous fluids, the caecostomy continued to drain well, and the Paul's tube came away 12 days later. The ovarian tumour was multilocular with numerous wart-like growths on its inner surface, and contained a thin mucinous fluid. Microscopically it proved to be a papillary cyst adenocarcinoma of the ovary.

At a second operation, 1 month after delivery, a total hysterectomy and right salpingo-oöphorectomy was performed, followed by resection of the growth from the sigmoid colon with end to end anastomosis.

Examination of the uterus revealed the remains of the placental site, but no evidence of malignancy. The colon showed ulceration of the mucosa completely encircling

the lumen which on section proved to be an adenocarcinoma extending right through the intestinal wall. It was considered that the ovarian tumour was not secondary to the intestinal neoplasm.

After a stormy convalescence, in which a faecal fistula developed, the patient made a reasonable recovery, though the fistula continued to drain. On 12th October laparotomy was undertaken in an attempt to mobilize the anastomosis and repair the fistula. This could not be done but a biopsy taken from the edge of the opening in the bowel proved not to contain any malignant tissue. Later the caecostomy and the fistula gradually closed, and when seen in the last 2 weeks, the patient's condition was good.

In conclusion, Mr. Steptoe suggested that persistence of symptoms of the type described should suggest the diagnosis of malignant colon, and the suspicion should lead to sigmoidoscopy and barium X-ray examination. The problem of treatment would depend on

(1) Can the survival of both mother and infant be secured?
(2) If one of the pair has little, if any chance of survival, how can the life of the other best be protected?

In inoperable cases a colostomy will often allow the mother to survive some time and normal labour ensue.

In operable cases the operative mortality and complications have to be considered. If the infant is viable and the lesion is sited in the pelvis or near the pelvic brim, resection together with Caesarean hysterectomy is probably indicated. If the lesion is in the transverse colon, resection with induction of labour would probably be safe. Better pre- and post-operative treatment, the use of chemotherapy and blood transfusions have reduced the risk of colonic operations in recent years. It may, therefore, be anticipated that energetic investigation and treatment of these cases will result in a marked reduction in both the maternal and foetal mortality.

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Mr. J. B. Cochrane described a case of

Malignant Ovarian Tumour Complicating Pregnancy

Mr. Cochrane said that the possibility of an ovarian tumour in pregnancy, occupying the pelvis, thereby obstructing labour, always receives due recognition, but that this tumour should be malignant featured less often principally on account of its infrequency.

Mr. Cochrane's case was a young primigravida of 24 years who expected her confinement on 19th October, 1952. She had booked a midwife for home delivery and received her antenatal supervision from her doctor.

In view of the non-engagement of the foetal head, the patient was referred to Mr. Cochrane's clinic when some 35-weeks pregnant. There an ovarian cyst was found by the registrar, obstructing the descent of the foetal head, and she was advised hospital confinement as Caesarean section was probable. Her haemoglobin level was 7·6 g. per cent and a course of intravenous iron was given.

Two weeks before term the membranes ruptured spontaneously, and Caesarean section was performed, a live male infant, 6¼ pounds in weight, being delivered without difficulty. On closing the uterus, a multilocular cyst was found arising from the left ovary, and one area of it was noted to have a degenerated appearance. It was thought possibly to be malignant but as the other ovary was normal and no glands were palpable it was thought prudent to remove the tumour and the left tube only.

Histological examination showed anaplastic carcinomatous cells to be present, and this opinion was confirmed by Dr. Paine of Sheffield who reported: "A very undifferentiated epithelial tumour judged to be highly malignant, though picture possibly vitiated by pregnancy. Probably a primary ovarian tumour of the type classified as sero-anaplastic adenocarcinoma."

Mr. Cochrane discussed the findings with the husband and wife and, after blood transfusion, he undertook a further operation and removed the uterus and right appendage. Fresh adhesions were present and on separating these two hard glands were felt in the left pedicle. No other evidence of metastases was present. The patient's recovery was uneventful, but histological section showed definite malignant growth remnants in the ovarian pedicle.

Mr. Cochrane had seen the patient at intervals since the extirpation 2½ years ago, and he felt that although the prognosis must still be guarded it would be fair to preserve an optimistic outlook.

Discussion

The two cases reported above were discussed together.

Mr. Malkin had seen a patient 25-weeks pregnant who developed peritonitis which at first settled on treatment. She was later found to have an inoperable carcinoma of the rectum.

Professor Russel had had experience of two cases of malignant disease of the alimentary tract associated with pregnancy. The first had a carcinoma of rectum, the second bilateral Krukenberg tumours. The latter patient had been admitted with post-partum eclampsia.

Mr. Madden had also seen two cases. His first patient had a carcinoma of pelvic colon. She was delivered by Caesarean section, and a colostomy performed. At a later stage the growth was resected and the uterus removed. His second case was also delivered by abdominal section. A rectal carcinoma lay below the presenting part. Palliative colostomy only was possible. The patient died in about 6 months.

Mr. Dickson also reported a case where a lower bowel tumour was associated with pregnancy.

Mr. Malpas introduced a note of reassurance. He had not seen a tumour of the lower bowel associated with pregnancy.

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

APRIL 1955

A Meeting of the North of England Obstetrical and Gynaecological Society was held in Leeds on Friday, 15th April, 1955.

Mr. H. A. Kelsey reported

A CASE OF HYDROCEPHALUS WITH A VERY HARD SKULL

Mr. Kelsey's patient was a primigravida of 32 who had been married 7 years. Pregnancy was normal until the 34th week when external cephalic version was performed on account of a breech presentation. At the 37th week the head was very high, and though on vaginal examination the pelvis seemed roomy the head could not be made to engage by fundal pressure. The head seemed larger than normal. An X-ray pelvimetry and cephalometry was performed and this showed foetal hydrocephalus to be present and a doubtful deformity in the lumbo-dorsal spine. The maternal pelvic measurements were of average proportions.

The patient was admitted for induction of labour. Vaginal examination revealed the cervix long and tightly closed, and, as labour did not commence after two courses of quinine sulphate, the patient was allowed home. As labour had not occurred by the 42nd week, and the cervix was soft and admitted a finger, the patient was readmitted for surgical induction of labour. There was gross disproportion but the head felt very hard and there was no eggshell crackling.

A further X-ray examination showed definite hydrocephalus, with the occipito-frontal diameter 14 cm. compared with 13·2 cm. at the 38th week.

It was, therefore, decided to perform surgical rupture of the membranes and craniotomy. Under a general anaesthetic the disproportion was confirmed and the forewaters were ruptured. A narrow trocar and canula was then inserted into the skull through the sagittal suture. The procedure was quite difficult as the parietal bones were very hard and the suture was narrower than the thickness of the canula. More than 10 ounces of cerebro-spinal fluid were released. The cervix was then stretched digitally to admit 2 fingers and the head was perforated but it was not possible to reduce the size of the head very much. It was hoped that in labour the head would mould following the perforation but it was still free at the end of the operation.

Uterine contractions commenced 9 hours after the operation. Good contractions occurred and the patient was given morphine. After 5 hours in labour the cervix was three-quarters dilated, but the head was still not engaged. It still felt very hard and its size did not seem to have been reduced at all by moulding. Mr. Theobald, who now saw the patient, considered that engagement was unlikely to occur and that there was considerable risk of rupture of the lower uterine segment. Another anaesthetic was, therefore, given and the foetus was extracted after the head had been crushed using a three-bladed cephalotribe. The head was extremely hard and difficult to crush, and the foetus showed a lumbar meningo-myelocele. The mother made a satisfactory recovery.

On inspection of the skull bones there were some typical thin lacunae, but these were only small in area. There were numerous thick bony ridges, the thickest being 0·12 inches. The skull was measured at 10 points on different bony ridges and the mean thickness was ·08 inch. According to Macdonald (1954) the mean thickness of the parietal bone in normal foetuses at term is ·003 inch. Mr. Kelsey had found no reference to hydrocephalus with this type of skull in the textbooks.

The only reference that he had been able to find was a passage in *The Pathology of the Fetus and Newborn* by Potter (1952) who wrote: "The skull may not be enlarged even though the ventricles are distended with fluid. The bones may be little more than thickened membranes or they may be thicker having irregular inner ridges separating small round or oval defects."

Mr. Kelsey expressed his appreciation to Mr. Theobald for permission to report this case.

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Macdonald, I. (1954): *J. Obstet. Gynaec. Brit. Emp.*, **61**, 253.

Potter, E. L. (1952): *Pathology of the Fetus and Newborn.* Yearbook Publishers, Chicago. p. 426.

Discussion

Mr. T. B. Fitzgerald had seen a similar case at University College Hospital. Caesarean section was performed as it was felt that craniotomy would be difficult. Mr. Fitzgerald asked if, in view of the difficulty in performing craniotomy, Caesarean section would be done in another such case.

Dr. R. Newton said that Dr. Hartley of Manchester had made a special X-ray study of abnormal foetal skulls and of the development of foetal skulls. In his M.D. thesis Professor Donald had advised delivery of the child as a breech and perforation of the hydrocephalic skull through the mouth.

In his reply Mr. Kelsey still favoured vaginal delivery.

Mr. S. B. Herd reported a case of

STATUS EPILEPTICUS IN PREGNANCY WITH UNUSUAL FEATURES

Mr. Herd said that this condition had occurred in a primigravida aged 22 who gave a long history of epilepsy with infrequent fits apparently well controlled by Epanutin and Phenobarbitone, for there had not been a fit for a year prior to her first attendance at hospital.

She was sent to hospital as a case of threatened abortion in March, 1953, but was then found not to be pregnant. Pregnancy must have commenced on her return from hospital and, when seen in August, she was found to be at the 5th month and apparently progressing normally. As the pregnancy advanced she did have more frequent fits and sustained several injuries and burns as a result. Otherwise her condition remained satisfactory until 1st January, 1954 when she was sent into hospital

as an emergency case of status epilepticus. A semi-comatose condition was present with severe and frequent fits. The blood pressure was 190/108 with a heart rate, just after a fit, of 120. The urine was clear of albumen. The fits were apparently typical and, in spite of very heavy administration of soluble phenobarbitone and paraldehyde, became almost continuous during the ensuing 24 hours.

On the following day there was hyperpyrexia, a steadily increasing tachycardia and the foetal heart was noticed to be irregular and uncountable. The urgent question of emptying the uterus arose, but early in this 2nd day contractions were noted, and by 3 p.m. labour had advanced to full dilation so that low forceps delivery, with episiotomy, of a stillborn child was possible, no anaesthetic being necessary. No further fit occurred, the last recognized convulsion having been 10 hours before delivery.

On the next day (3rd January) the patient was still deeply unconscious so that superimposed meningitis was considered but excluded by examination of the C.S.F. Consciousness returned on the 4th morning and the sedation was discontinued, but tachycardia and pyrexia persisted. On the 5th day sudden severe collapse occurred and there was then found to be extreme tenderness in the left iliac fossa although no abdominal distension or abnormal dullness. There was slight response to intravenous therapy, but aphasia and right hemiparesis of the face were noticed. Further collapse was followed by death within 5 hours of the initial collapse—the cause of death being then thought to be the result of heavy sedation plus the post-epileptic state.

Post-mortem examination revealed rupture of the oesphagus and stomach with rupture of the diaphragm and herniation of two loops of small intestine, a part of the large intestine, the spleen and the tail of the pancreas into the thoracic cavity. There was considerable digestion and necrosis from stomach contents.

Mr. Herd commented on the combination of epilepsy and pregnancy, and the indications for termination of the pregnancy, also the relation between status epilepticus and the lesions found. He said there is a known relationship between rupture of the oesophagus and major epilepsy, and in his case the rupture extended to the stomach and the diaphragm. Pregnancy would favour such a development as the pressure of the fundus in the late months would act as a further factor. He had found no reference to the association of the three conditions described. Epilepsy in pregnancy may be improved, in other cases attacks are more frequent and in some status epilepticus has been described. Pregnancy may even be the exciting cause of epilepsy.

Status epilepticus in pregnancy endangers the life of the child and Caesarean section may be indicated—the mother is said to die whatever form of treatment is given (Kretzschmar, 1930). Mr. Herd commented on the remarkable feature in his case: the survival of the patient for so long after the lesions had developed. There was no sign of pneumothorax such as might have given an early indication of the rupture, and if the diagnosis had been possible the prognosis for operation would have been quite hopeless. It would seem that immediate emptying of the uterus on development of status epilepticus may be advisable for the child's sake and often the only hope of saving the mother's life and that a slender one.

Reference

Kretzschmar, N. R. (1930): *Amer. J. Obstet. Gynec.*, **19**, 557.

Discussion

Mr. P. C. Barkla had had a patient in his care who developed 50 fits in 45 hours and was for many hours in status epilepticus when 32-weeks pregnant. She improved and did well until the 39th week when she was delivered normally of a live child.

Mr. F. Stabler said that fluid retention may precipitate fits and one reason for fits being noticed at the time of menstruation is the association of fluid retention.

Mr. G. W. Theobald asked if it would not be logical to give curare. He pointed out that the oesophagus ruptures with epilepsy and not with eclampsia.

Mr. H. Agar said that the reason for the foetal death was not explained, and it might be due to cyanosis of the mother and anoxia of the foetus.

In his reply Mr. Herd said that the patient did become cyanosed but there was no evidence of oedema.

Mr. Herd described a case of

Incarcerated Foreign Body in the Vagina

The patient was a married woman of 24 who gave no history of past pregnancies, illnesses or operations. She was referred to a surgical clinic with a complaint of intermittent pain in the right hypochondrium for 3 years. The pain was not related to menstruation but occurred mainly after defaecation and there had occasionally been passage of blood per rectum. She had intramenstrual dysmenorrhoea, scanty periods and occasionally an offensive discharge.

The surgeon considered her to have appendicitis, but a straight X-ray showed a "front collar stud" in the pelvis, and the patient was, therefore, referred to Mr. Herd. No history of interference or insertion of the foreign body could be obtained.

Pelvic examination showed a normal vaginal introitus, a short vagina, and a supple thin transverse septum 2½ inches from the introitus, with a very fine opening which barely admitted a probe but which dilated quite easily revealing the stud in the upper compartment of the vagina. The septum was widely excised, and the patient became pregnant within 3 months and had a normal delivery of a full-time child.

The stud was of brass, much encrusted, and had a bone base which was corroded away proving that the stud had been *in situ* many years.

It was thought that the septum might be the result of infection and irritation of the stud, introduced in childhood and its presence forgotten. The abdominal pain was apparently not related and early pregnancy proved the absence of ascending infection.

Mr. J. W. Hunter had seen a child of 8 years with a chronic discharge. It was his practice to have an X-ray for all children, and in this case a front collar stud was found.

Mr. C. E. B. Rickards raised the question of the transverse septum. He had excised a similar septum in a girl who subsequently had a normal delivery.

Miss C. H. Peaker mentioned 2 cases where a transverse septum had been present.

Mr. F. E. Stabler thought that the septum was a congenital diaphragm and not produced by irritation. He too had seen a front collar stud in the vagina in a child.

Other members of the Society had seen articles ranging from a piece of tin to a gold fish.

Mr. R. F. Lawrence recorded a case of

Multiple Primary Carcinomata

In his Linacre Lecture on "Multiple New Growths" Murray (1927) points out that primary multiplicity is so common in benign neoplasms that it is frequently regarded as presumptive evidence of the benign character of the new growth in which it is encountered.

The malignant growths are usually solitary and the late occurrence of multiple foci is most frequently due to dissemination of living cells from the primary focus. He quotes the criteria of multiplicity of malignant new growths laid down by Billroth in 1880:

(1) The tumours have different structures.
(2) Each tumour could be derived histogenetically from its own mother tissue.
(3) Each tumour produced distinctive metastases.

The standards are high and Welch (1954) following Warren and Gates (1932) has suggested different criteria.

The calculated incidence of multiple primary malignant neoplasms will depend on the criteria adopted: on whether skin lesions and lesions of paired organs are included: on whether metachronous as well as synchronous lesions are included and on whether the calculation is based on necropsy material.

Murray quotes Puhr's series of 1,559 cases with tumours found at necropsy, and of these 219 cases presented multiple growths, but only 5 cases were of multiple malignant growths. Egli found 20 cases of multiple malignant growths in 966 cancer autopsies—Harbitz 32 in 524 cases. Warren and Gates reported the incidence of multiple primary malignancies as 3·7 per cent, and Welch mentions figures ranging between 0·3 per cent to 6·8 per cent. Triple primaries are occasionally reported. Marrangoni and McKenna (1952) mention 2 cases with primaries in breast, sigmoid and uterus, and in uterus, ovary and colon. Cahan and others (1950) found one case with primaries in breast, rectum and lung, and Spain (1949) with primaries of bronchus, pancreas and prostate. Warren and Ehrenreich (1944) in 194 cases of multiple malignancy include 29 cases with 3 or more primaries.

This patient first came under observation in 1945. She was a married woman aged 45 years, with one child. In June, 1945 she sustained a slight injury and became aware of a lump in both breasts. She immediately consulted her doctor and without delay simple amputation of the right breast was performed. This tumour was reported to be a carcinoma and as a result simple mastectomy was done on the left side, the tumour being found to be a sarcoma. She was then referred to the Radiotherapy Centre and a course of deep X-ray given. Radical mastectomy with removal of the axillary glands and further deep X-ray therapy were adopted and apart from some pelvic pain in 1946 the records revealed nothing of interest.

The patient came under Mr. Lawrence's care in November, 1949 when she gave a history of frequent and prolonged periods for 3 months. She had noticed abdominal swelling for 2 weeks and attacks of colicky abdominal pain for a considerable time. Free fluid was detected, and on vaginal examination a large fixed mass was felt behind the uterus.

Laparotomy revealed large quantities of ascitic fluid with nodules scattered over peritoneum and omentum. Both tubes were thickened and the left ovary involved in a mass of neoplastic tissue attached loosely to the pelvic colon. The right ovary was large but not obviously abnormal. Bilateral salpingo-oöphorectomy was performed, and, as the tumour was reported a papilliferous adenocarcinoma, further deep X-ray therapy was given. Treatment was complicated by leucopenia, and despite temporary benefit she died 8 months after laparotomy.

Pathology

The tumour in the *right breast* was a characteristic scirrhous carcinoma. Genesis of malignant growth was seen in many small ducts filled with rather small tumour cells, with eruption into the surrounding stroma to form a moderately cellular, infiltrative spread. Mitotic figures are not very numerous. The *left breast* showed a sarcoma of spindle-cell structure. The tumour varies in different areas but all parts show active growth with numerous mitotic figures. A striking feature was the perivascular architecture with intervening necrosis. No glandular elements were present, benign or carcinomatous, but the layout of the tissue suggests origin in an intracanalicular fibroadenoma.

The report on the ovarian tissue was that the section showed a highly intricate papilliferous type of adenocarcinoma. The cells were polyhedral and showed large numbers of mitoses. In some areas the architecture was similar to a papilloma of the bladder and in others resembled a serous ovarian cystadenoma with numerous "psammoma" bodies. No resemblance between the ovarian tumour and either of the breast tumours could be found.

Mr. Alan Brews was asked to review the case and submitted the slides to Dr. W. W. Woods who agreed that the ovarian neoplasm had no relation to the mammary neoplasms. He stated that "the growth seems to have arisen from the outer surface of each ovary leaving a large central area of normal ovarian tissue. In the section of the right breast there is an ordinary small polygonal-celled scirrhous carcinoma, and the

section from the left breast contains a rare neoplasm that is difficult to classify; it is difficult to deny that it is a polymorphic-celled carcinoma.

"This is rather an amazing trio of separate independent primary carcinomata."

At the same time Professor Dorothy Russell also examined the sections and endorsed Dr. Wood's report in its entirety.

Conclusion

This case is presented as a pathological curio, and it is not suggested that it has any particular clinical significance, but it may be opportune to mention here that in their classic paper Warren and Gates draw the following conclusions:

(1) Multiple cancers occur at approximately the same age as single cancers.
(2) Multiple malignant tumours occur more frequently than can be explained on the basis of chance.
(3) This may be explained by a predisposition or susceptibility to cancer in certain persons, or to the action of some factor favouring the development of malignancy.

My thanks are offered to Dr. E. K. Dawson and Dr. R. B. T. Baldwin for the original reports, to Dr. W. W. Woods and Professor Dorothy Russell for reviewing the histological features, to Dr. Magnus Haines for his advice and technical aid, and to Mr. Alan Brews for permission to make use of his notes.

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Marrangoni, A. G., and McKenna, R. (1952): *Amer. J. Obstet. Gynec.*, **63**, 660.
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Spain, D. M. (1949): *N. Y. St. J. Med.*, **49**, 1445.
Warren, S., and Ehrenreich, T. (1944): *Cancer Res.*, **4**, 554.
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Welch, J. W. (1954): *J. Kansas med. Soc.*, **55**, 314.

Discussion

Mr. C. J. Dewhurst had seen an adenocarcinoma in an appendix unrelated to a second carcinoma in the uterus.

Mr. S. B. Herd had had a patient in whom a carcinoma in the pelvic colon, and later of the ascending colon, had been removed by a surgeon. At the earliest sign of post-menopausal bleeding, the uterus was removed and a very early adenocarcinoma found, but she developed a pelvic recurrence probably because of a tendency to carcinoma.

Miss C. Bates had a patient in her care for whom she had removed a malignant ovarian tumour. At a second laparotomy a large tumour was found in the transverse colon unrelated to the ovarian carcinoma. She now had a recurrence in the pelvis.

Mr. T. Redman mentioned a girl of 28 in whom a carcinoma had been found in breast and caecum.

The President had repaired a prolapse in a woman of 77 who had been operated on for carcinoma of the colon and an epithelioma of the vulva. At the age of 93 she broadcasted.

Mr. H. A. Kelsey referred to a case of malignant ovarian tumour. Intra-uterine radium was used following removal of the ovary, and later a carcinoma of the body of the uterus developed.

Mr. J. W. Hunter mentioned the difficulty in histology, and that the appearance may vary in different areas. He had removed a malignant ovarian cyst in a girl of 22. Three years later a pseudomucinous cyst and the uterus were removed, but after 4 years she had a recurrence with ascites.

Other members of the Society had seen similar cases.

BOOK REVIEWS

"British Obstetric and Gynaecological Practice." Edited by SIR EARDLEY HOLLAND and ALECK BOURNE. William Heinemann Medical Books Ltd., London, 1955.

"Obstetrics." Edited by SIR EARDLEY HOLLAND. Pp. xiv+1166, with 395 illustrations. Price 115*s*.

"Gynaecology." Edited by ALECK BOURNE. Pp. xii+840, with 363 illustrations. Price 95*s*.

THESE two large volumes amply fulfil the claim of the two distinguished editors that they present an authoritative statement of British obstetrics and gynaecology. In the choice of contributors the editors have obviously and wisely been guided by a desire to select the younger workers. This is wise because within a few years any textbook becomes out of date and the responsibility for continuing revision must inevitably rest largely with the younger authors. This consideration raises at the outset the question of the expediency in these days of rapid change in the art and science of obstetrics and gynaecology of the textbook, which in size and coverage assumes the character of an encyclopaedia. Here the mere bulk militates against the frequent revision which is imperative in these days of rapid progress unless, as we have witnessed in the case of other publication enterprises, this is met by the issue of frequent supplements. It raises inevitably the question of the comparative value for the average reader of the large and expensive volume as against that of moderate size.

Of the average standard of the contributions we have nothing but praise. The claim of the editors that the volumes are "in essence clinical and practical" is well justified.

In the Obstetrics volume there are excellent sections dealing with the new concepts of normal and incothe nate uterine action. There is a masterly chapter on ordiToxaemias of Pregnancy but, alas, in its discussion on aetiology it achieves little more than to testify to the ever-increasing complexity of the theorizing that envelopes this subject. In the chapter on The Normal Puerperium it is stated that Haig Ferguson of Edinburgh was amongst the first in this country to advocate early rising after childbirth. We have always associated Haultain (senior), also of Edinburgh, with this advocacy. The chapters on Tuberculosis and Heart Disease in Pregnancy give valuable summaries of the present position of these matters. In the Tuberculosis chapter, in a reference to the well-known observations at Black Notley Hospital, it is stated that the "proportion of retrogressions (i.e., in pregnant tuberculous women) was no more than would have been expected in a comparable group of non-pregnant tuberculous women under similar conditions". No qualifying reference is made to the difficulty in this case of obtaining valid controls for it may be urged that in the same age-group the tuberculous women who are pregnant are on the average likely to be more vigorous and less advanced in the disease than those who are not pregnant.

With multiple contributors there is the risk of sharp differences of opinion creeping in. We have, in these volumes, found little evidence of this. There is also the editorial responsibility of maintaining an equitable balance between the different sections. This also has, on the whole, been well looked after. Here and there, however, we have detected some evidence of editorial remissness. The contributor of the excellent chapter on the diseases of the Corpus Uteri gives no description of the techniques of hysterectomy "as these are described in the various textbooks of operative gynaecology". This consideration, however, does not commend itself to other contributors. Thus in the section on Prolapse there is a full description of the Manchester operation and in the section on Fistula a full account of the relevant operation.

In two different sections haemorrhage at the menopause is dealt with at some length by two contributors whose discussion of treatment is somewhat at variance. It must also seem a rather strange classification which includes Dysmenorrhoea under the section on Abnormal Uterine Haemorrhage.

There are some important conditions that do not appear at all. For example, despite their frequency and their gynaecological importance in some of the British Colonies there is no mention of Granuloma Inguinale or Lymphopathia Venereum. Further, despite the great interest being roused by the World Health Organization in the treponematoses, there is no reference to so-called Extra-venereal Syphilis and its gynaecological manifestations.

Finally we would congratulate publishers and editors on the format of the volumes, on the excellence of the illustrations, of the paper and of the printing.

"The Lower Parts of the Uterus during the First Stage of Labour in Occipito-Anterior Vertex Presentation. Studies by Means of Intrauterine Tokography." By L. LINDGREN. Pp. 79, with 32 figs. and 15 refs. Reprint from the *Acta Obstetrica et Gynecologica Scandinavia*, Vol. 34, Supp. 2. Stockholm, 1955.

THIS monograph of 79 pages from the gynaecological department of Sabbatsberg Hospital, Stockholm, deals with the results of intra-uterine tokography. The method employed, including sources of errors and their evaluation, is described in detail and with clarity.

The sensitive part of the tokograph consists of a strain gauge enclosed in a circular chamber 18 mm. in diameter. The sterilized instrument, containing four such chambers, is introduced through the cervix and placed between the foetal membranes and the uterine wall. The sensitive part of the uppermost chamber faces the foetal membranes in the body of the uterus, and records

"amniotic pressure"; the sensitive parts of the three lower chambers face the uterine wall in the lower part of the uterus at varying levels in relation to the presenting foetal head, and measure the "pressure of the uterine wall".

Thirty-five women, aged between 18 and 37 years, 23 of them primigravidae, were investigated during the first stage of labour.

Three different types of tracing were obtained. In the first type the peaks of pressure of the uterine wall at the level of the greatest circumference of the foetal head coincided with the peaks representing the rise of amniotic pressure during each uterine contraction. In the second type of tracing small oscillations, termed "P waves", were superimposed on the tracing of the pressure of the uterine wall at the level of the greatest circumference of the foetal head during and between the uterine contractions. In the third type small oscillations occurred in these tracings, only during uterine contractions; they were also seen in the tracings of amniotic pressure. The third type of tracing was grouped together with the first type because it was thought that these oscillations were due to fluctuations in the amniotic pressure as the result of disturbances caused by gliding of the instrument.

Tracings of the first (and third) type were obtained in 19 cases and were termed "non-spastic"; tracings of the second type were found 16 times and were called "spastic".

In the first group 3 patients had no pain at all, and only 5 of the remaining 16 had some pain between uterine contractions. All patients in the "spastic" group suffered from severe distress during and also between uterine contractions. The pains, and the P waves, could be made to disappear by local injection into the lower part of the uterus of adrenaline, whilst local injection of "lidocaine" (called "xylocaine" in this country) abolished the pain but not the P waves. The P waves are thus regarded as the manifestation of local contractions of the circular muscle fibres which act as a sphincter, as described by Goerttler.

In the "spastic group" the amniotic pressure between uterine contractions was 25 per cent higher, the pressure of the uterine wall at the level of the greatest circumference of the foetal head was 50 per cent higher during contractions, the muscle tone at that level was 100 per cent higher between contractions, and the rate of dilatation of the cervix was 50 per cent slower, as compared with the "non-spastic" cases.

In the lower part of the cervix no active contractions could be registered by intra-uterine tokography. This is in accordance with the facts that there are only longitudinal muscles in that area, that there are only small amounts of actomyosin (a group of proteins responsible for uterine contractions) in the cervix, and that no action potentials could be detected in the lower cervix by means of electrohysterography.

N. Alders

"Backache in Women." By E. SCHLEYER-SAUNDERS, M.D., F.I.C.S. With a Foreword by W. C. W. NIXON, F.R.C.S., F.R.C.O.G. Pp. 80, with 6 figs. John Wright & Sons, Ltd., Bristol, 1955. Price 7*s.* 6*d.*

THIS small volume is a useful survey of the clinical features, diagnosis and treatment of the many and various conditions that produce backache in women. The subject is discussed under three main headings: gynaecological, orthopaedic and so-called rheumatic, and there are minor groups connected with intestinal and urinary disorders. The examination procedure is fully described and the management of the various conditions is orthodox and straightforward. The book reflects the wide experience of the author and the deep thought he has given to the subject.

Here and there he makes a fresh point. He cites the case of a woman who married a farmer and who discarded the high-heel shoes she had been accustomed to wear in town. He advised her to revert to high heels and this cured the backache. He sounds a warning in regard to exercises in the puerperium and records a case of protrusion of a lumbar disk that occurred during such an exercise involving forward bending.

In his section on Posterior Parametritis the author reflects clearly the influence of German gynaecologists and especially Martius of Göttingen. Though he does not mention his German authorities he obviously has in mind the condition described by Martius as "parametropathia spastica", i.e., a spastic state of the unstriped muscle in the true pelvis which is a common cause of pain from the tender bands produced in the utero-sacral and lateral parametrium. This condition has received little attention in English literature though Young in this country and Howard Taylor in America have emphasized its importance. Martius and others believe it often to have a psychosomatic origin.

In some respects this book is unsatisfactory. There is a tendency to uncritical statement. He says: "I still remember the time when every woman who complained of backache was considered to have a displaced uterus and was advised to have it corrected by an operation." In one place he states it is possible to pick out women *prone* to backache by watching their gait, how they sit down, etc., whilst in another place he infers that the value of such observations is found in the case of women who *actually have* backache.

REVIEW OF CURRENT LITERATURE

CONTENTS

	REF.
PHYSIOLOGY	142
PREGNANCY	143
LABOUR	158
OBSTETRICAL OPERATIONS	163
MATERNAL MORTALITY	164
INFANT	165
GYNAECOLOGY	170
New growths of the reproductive organs	178
Operations	189
Urology	196

PHYSIOLOGY

142. **Hormone Effects on Basal Body Temperatures and Menstrual Patterns.**

By R. H. PERLMAN. *West. J. Surg. Obstet. Gynec.*, 63, 116–122. Mar. 1955. 4 charts. 11 refs.

The author administered thyroglobulin, testosterone, oestrone and radio-iodine (I_{131}) to various patients and observed the effect on basal temperature charts. Oestrone and progesterone do not appear to alter the basic shape of the charts but thyroid and radio-iodine produce a "biphasic curve" which approximates to the normal. The author advocates the use of the basal temperature chart as a simple aid to indicate the relative states of hormonal balance.

[This paper is very difficult to understand and the data presented do not appear to justify all the author's contentions.] *D. C. A. Bevis*

PREGNANCY

143. **Vaginal Smears and the Diagnosis of Pregnancy.** (Diagnostic de grossesse et frottis vaginaux.)

By A. LAFFONT and R. BOURGAREL. *Gynéc. Obstét.*, 53, 529–534. 1954.

The writers draw attention to the practical value of the vaginal test in the diagnosis of normal pregnancy, being a rapid and simple method compared with the more costly and elaborate methods. The sample must be entirely vaginal and must not contain any cervical elements, blood, nor discharge. It is best obtained by suction with a glass pipette fitted with a rubber bulb. The spreading on a slide must be quick and the slide should be immediately plunged in equal parts of ether and alcohol—remaining in this till staining by Isaac and Wurch's method is started. This method in wet smears is used for the study of the cells. A second smear, used dry, is stained by Gram's method for a study of the vaginal flora and finally the pH is estimated.

The writers collected 50 results, all recent ones and taken at random. They were classified as follows:

(1) Ten normal pregnancies at different stages.

(2) Six unstable pregnancies rendered secure either spontaneously or by treatment.

(3) Four carneous moles.

(4) Eleven abortions at different stages, the smears being taken before or during miscarriage.

(5) Nine complete abortions, the smears being taken after spontaneous completion or curettage.

(6) Five cases of excessive bleeding following a period of amenorrhoea where the differential diagnosis between threatened miscarriage and amenorrhoea not due to pregnancy was difficult. These proved later not to be pregnant.

(7) Three cases of postmaturity.

In normal pregnancy, although the period of gestation varied between 3 weeks to 9 months, the uniform results were:

pH always below four.

Eosinophils varied between 2 and 8 per field.

Cells showing pycnosis were between 6 and 25 per field.

Pregnancy navicular shaped cells occurred in bundles and in large numbers.

Abundant evidence of progesterone reaction.

Vaginal flora: almost pure cultures of Döderlein bacilli.

In other words the picture in pregnancy is typical and resembles no other vaginal smear in cases of amenorrhoea. In cases of doubt repetition is a simple matter.

The writers describe in detail the microscopic findings in the 6 other groups of cases mentioned.

In their opinion an increase in the number of eosinophil cells is a danger sign and indicates the ovum is threatened or dead.

Further, in cases of threatened abortion a favourable prognosis can be given if the number of eosinophils per field does not exceed 10 per cent whatever be the number of pycnotic cells.

The writers conclude by saying that, although the vaginal smear method is not infallible, it is a sufficiently reliable guide to confirm a clinical diagnosis, to establish prognosis, or to indicate the appropriate therapy.

D. Maxwell

144. **Clinical Experiences with Soft-Tissue Placentography.**

By R. PERCIVAL and S. MURRAY. *Lancet*, **1**, 1045–1051. May 21, 1955. 3 tables. 8 refs.

The authors record their observations of soft-tissue placentography in 275 cases of pregnancy where there was ante-partum haemorrhage, unexplained displacement of the presenting part, unexplained breech presentations, unexplained failure of version or other conditions. The most important indication for placentography was ante-partum haemorrhage where the precise position of the placenta was in doubt. Of 50 cases of placenta praevia only 1 was missed. Fourteen of these 50 cases were diagnosed by placentography before any bleeding took place and were X-rayed purely on the grounds of abnormal relationship between the presenting part and the pelvic brim. There were 84 cases of ante-partum haemorrhage not due to placenta praevia. Only 2 cases were incorrectly diagnosed. The authors stress that before about the 34th week precise diagnosis can be made only where the placenta is implanted mainly around the fundus or mainly in the lower segment. Even when the placenta appears to extend from the upper part of the uterus down into the pelvis, at this early stage it is impossible to predict how much will remain there as the uterus grows and the lower segment forms. They point out that the advantages of this aid to diagnosis are greatest in the conservative management of ante-partum haemorrhage.

H. H. Fouracre Barns

145. **X-ray Visualization of the Placenta.**

By H. G. WATSON. *West. J. Surg. Obstet. Gynec.*, **63**, 151–154. Mar. 1955. 9 refs.

Methods of radiological diagnosis of placenta praevia are reviewed and the results given using soft-tissue radiography. Three films are normally taken; a soft-tissue film of the lateral abdomen with the patient erect, a true lateral of the pelvis to judge anterior or posterior displacement of the presenting part in relation to the pelvic brim and an anterior recumbent film of the abdomen to supplement the other two; occasionally oblique views are needed when the placenta cannot be demonstrated. A positive diagnosis was made in 19 cases and confirmed in 17; placenta praevia was correctly excluded in all of 42 cases.

[Full technical details of the radiological methods are given in the discussion which followed the presentation of this paper to the Pacific Coast Obstetrical and Gynecological Society.] *D. C. A. Bevis*

146. **The Effect of Promethazine in Nausea and Vomiting of Pregnancy.**

By J. P. B. FITZGERALD. *N.Z. med. J.*, **54**, 215–218. Apr. 1955. 16 refs.

In a series of 254 clinic patients at Aberdeen the incidence of vomiting and nausea was 61 per cent. Fifty-eight patients were treated with promethazine (89·6 per cent cured or improved) while a control series of 56 cases was treated with ascorbic acid. In the control group 28·5 per cent were cured or improved.

L. Woodrow Cox

147. **Potassium Depletion and Replacement in Hyperemesis.**

By J. P. B. FITZGERALD. *N.Z. med. J.*, **54**, 36–50. Feb. 1955. 9 refs. 10 figs.

A study of 10 cases with severe hyperemesis in early pregnancy is recorded. Haemoglobin, plasma protein, plasma potassium and chloride were estimated every 24 or 48 hours. Potassium deficiency was observed, and replacement of this ion was undertaken in the course of the intravenous infusion for treatment of dehydration. The author's impression was that convalescence was shortened and vomiting ceased sooner when potassium salts were given. Full clinical and laboratory details of each case are given in an appendix. The cases were severely dehydrated on admission to hospital, and vomiting continued for several days after admission, and the normal treatment with promethazine intramuscularly, plasma infusion, and rectal chloral and bromide was given. A large controlled series would be necessary, however, to substantiate the impression gained that potassium deficiency retarded recovery.

L. Woodrow Cox

148. **Naucaine Therapy in Nausea and Vomiting of Pregnancy.**

By D. D. CURTIS. *Obstet. Gynec.*, **5**, 209–210. Feb. 1955.

The author reports on the use of oral Naucaine, a specially treated form of procaine hydrochloride, in 100

cases of vomiting of pregnancy. One tablet, or 4 ml. of the liquid preparation, was prescribed every hour until relief was obtained, up to 8 doses. Only one case showed sensitivity to the drug. Other cases started with 3 tablets followed by 1 every 30 minutes for 4 hours. All patients were urged to take frequent small meals.

In 88 per cent there was complete relief, in 95 per cent improvement and failure in 5 per cent.

J. G. Dumoulin

149. **Is the Use of Morphia Justified in the Medical Treatment of Eclampsia?** (Está justificado el uso de la morfina en la terapeútica médica de la eclampsia?)

By E. MORACCI. *Obstet. Ginec. Lat-amer.*, **12**, 539–546. Nov./Dec. 1954. 4 figs. 22 refs.

After referring to the medical treatment of eclampsia as advised by Stroganoff in 1897 and others, using morphia, the author discusses the experimental findings of Amantea, who, in 1920, observed that epileptic convulsions could be produced in 25 per cent of dogs by placing paper soaked with 1 per cent strychnine sulphate on the motor cerebral cortex. If however a subcutaneous injection of morphia was previously given to every dog, then 100 per cent of them would demonstrate epileptic convulsions under the same experimental procedure.

The work of two other writers, Fulchinioni and Neuwenhuyse, is mentioned. Each performed experiments on animals which led them to believe that morphia provoked epileptic crises when these animals were submitted to various types of stimulation. The observations of Gibbs, who showed that morphia given to epileptic subjects before an electro-encephalogram produced a characteristic curve in the tracings, are next mentioned, followed by reference to Maltby and Rosenbaum, who found that 65 per cent of eclamptic patients showed abnormal curves in an electro-encephalogram.

The author reports on his own findings using an electro-encephalogram on pregnant patients, whilst opening and closing their eyes. Various alterations in the tracings under these experimental conditions were observed, but it was only in the eclamptic patients that these abnormal tracings could still be found after delivery.

In view of these findings, the author maintains that morphia should not be used in the treatment of eclampsia, and illustrates how effective conservative treatment without the use of morphia can be, by reporting his own series of 30 cases of eclampsia: they all recovered with the exception of 2, who were in a comatose state when admitted and died shortly afterwards. His treatment consists of intramuscular injections of a 15 per cent solution of magnesium sulphate and also luminal. During the last 2 years he has been using, in addition, a substance called Cocarboxilasa, which is given by intravenous injection in doses of 200 mg. every 3 hours up to a total of 1·0–1·2 g. in a day. *John F. Foulkes*

150. **The Role of Vasodepressor Drugs in the Treatment of Toxemia of Pregnancy.**

By S. T. GARBER. *West. J. Surg. Obstet. Gynec.*, **63**, 201–204. Apr. 1955. 29 refs.

After reviewing recent views on the pathology of the toxaemias, the author (from the University of Cincinnati) classifies the vaso-depressor drugs:

(*a*) Veratrum alkaloids, phthalazine compounds and Rauwolfia serpentina. This group is believed to act on the hypothalamus or vasomotor centre. Good motor control is retained even with Rauwolfia which also brings about sedation and reduced emotional response.

(*b*) Spinal anaesthetics and autonomic blockading agents (tetraethylammonium bromide, hexamethonium, etc.). These drugs produce venous pooling and the postural hypotension precludes their use except in the supine position. They are of use in essential hypertension but produce little effect in pre-eclampsia.

(*c*) Peripherally acting drugs (Priscoline and dibenamine). Drugs acting on the nerve endings close to the neuromuscular junction.

(*d*) Adrenolytic substances (Regitine and benzodioxane), drugs used in the diagnosis of phaeochromocytoma.

Both these groups have been useful in studying the nature of the hypertension in toxaemia but are inapplicable in treatment.

The use of veratrum and, more recently, Apresoline, dispenses with the need for sedatives in the treatment of pre-eclampsia and eclampsia (magnesium sulphate is also used in eclampsia) and has resulted in a nil mortality from eclampsia in the Cincinnati General Hospital over the last 9½ years. *D. C. A. Bevis*

151. **Capillary Resistance During Pregnancy and the Significance of its Importance in Cases of Retroplacental Haematoma and Habitual Abortion. Treatment with Vitamins and Cortisone.** (La résistance capillaire au cours de la grossesse. L'intérêt de sa mesure et au cours de l'hématome rétro-placentaire et des avortements à répétition. Traitement vitaminique et cortisonique.)

By A. J. BRET and M. BARDIAUX. *Gynéc. Obstét.*, **53**, 618–639. 1954. 5 figs. 77 refs.

This is a long paper with 77 references including numerous ones to the English writers, Young, Sheehan, Bywaters and Beall. There are four convincing photomicrographs showing changes in blood vessels in cases of miscarriage.

The writers start by mentioning the work of Couvelaire in 1937, who concluded then that there were two factors necessary to bring about utero-placental haemorrhages: (*a*) a vascular predisposition and (*b*) a particular state of the neuro-vegetative system. Hypertension was not by any means the rule in these cases. Certain changes in the *capillaries* were common findings.

Nine factors, the writers consider, may modify capillary resistance:

(1) Substances associated with vitamin C.

(2) Vitamin E (α tocopherol).

(3) The antihistamines increase capillary resistance particularly in the presence of traumatic shock and are synergistic with vitamin C.

(4) Hypertension associated with instability of the serum protein affects the sensitivity of the renal capillaries.

(5) Under the influence of cold and trauma capillary sensitivity is altered.

(6) The sex hormones may rhythmically alter resistance in capillaries.

(7) In cases of accidental haemorrhage due to fibrinolysis or afibrinogenaemia, cortisone is probably an important factor in causing the fibrinogen to reappear in the circulation.

(8) The frequent association of lowered capillary resistance where there is excessive excretion of the 17-ketosteroids has been noted on many occasions.

(9) The good effect of cortisone on capillary resistance in cases of chronic purpura has often been spectacular.

The writers are convinced that there exists a group of patients who present constitutionally a definite capillary fragility and that different forms of placental apoplexy develop more often in these predisposed subjects. Reference is made to the work of Young in 1942, of Bywaters and Beall during the last war, and of Trueta on the effects of trauma on the kidney.

As regards prophylactic treatment, vitamin C, vitamin E and antihistamine drugs are all advised particularly in cases of habitual abortion.

Cortisone is also advised and any means to diminish too much excretion of the 17-ketosteroids. In certain cases, despite all these precautions, a Caesarean section prior to term may be justified.

D. Maxwell

152. **Fibrinogenopenia Complicating Pregnancy.**

By D. P. JACKSON, R. C. HARTMANN and T. BUSBY. *Obstet. Gynec.*, **5**, 223–247. Mar. 1955. 54 refs.

This report presents detailed clinical and laboratory observations on 10 patients who developed fibrinogenopenia during pregnancy. In 1 case there was bacteraemia associated with abortion, in 7 premature separation of the placenta (only 2 had toxaemia), in 1 prolonged retention *in utero* of a dead foetus, and in 1 amniotic fluid embolism.

Ten other patients with various complications of pregnancy including abruptio placentae and foetal death *in utero* were studied. None developed a coagulation defect.

Of the 7 cases with accidental haemorrhage, thrombocytopenia was demonstrated in 6 and a moderate reduction of prothrombin in 5; none showed increased fibrinolytic activity in the plasma. All received blood transfusions, and 2 were given fibrinogen. There was no fatality in this group. In the case with the retained dead foetus no evidence was found of increased fibrinolytic activity but it seemed to be present in the patient who died of amniotic fluid embolism. The patient with the septic abortion also died. Her blood showed bacteraemia, afibrinogenaemia, thrombocytopenia, hypoprothrombinaemia, but no evidence of increased fibrinolytic activity.

The authors feel that the mechanism for the production of the fibrinogen deficiency in their cases is the entrance into the maternal circulation of thromboplastic agents from the uterine contents.

J. G. Dumoulin

153. **Iron-Deficiency Anaemia in Pregnancy.**

By P. B. B. GATENBY and E. W. LILLIE. *Lancet*, **1**, 740–743. Apr. 9, 1955. 8 tables. 2 figs. 18 refs.

The authors record their observations on 1,027 patients (23 per cent of the pregnant women attending the hospital) with a haemoglobin value of less than 10 g. per 100 ml. which was the standard accepted as the lowest value which could be regarded as due to hydraemia. Of these, 347 patients were studied in detail and it was found that a third had no symptoms indicating anaemia. Only breathlessness seemed to have any relation to the haemoglobin level. The authors draw attention to the fact that it is unsafe to diagnose anaemia on physical signs alone. Two hundred and ten out of 385 cases (54·5 per cent) had signs of anaemia such as pallor of skin or conjunctivae. Haemoglobinometry is essential in diagnosis as well as assessing progress. Abnormal changes were found in the nails of 43 women (11·2 per cent). In reviewing the aetiology it was found that the incidence of severe anaemia increased with parity. Inadequate supply of elements essential for formation of haemoglobin was another factor. Little difference in response to ferrous sulphate and ferrous gluconate was found. The authors conclude that it seems reasonable and good practice to give an efficient preparation of iron to every pregnant woman in the last 12 weeks of pregnancy.

H. H. Fouracre Barns

154. **Varicoceles of the Round Ligament in Pregnancy Simulating Inguinal Hernia.**

By J. S. TOMKINSON and W. R. WINTERTON. *Brit. med. J.*, **1**, 889–890. Apr. 9, 1955. 2 figs. 4 refs.

The authors describe two cases seen at Queen Charlotte's Hospital, London, of varicoceles of the round ligament during pregnancy, which simulated inguinal herniae. In both cases there were associated varicosities of the vulva. In the first case the swellings subsided after delivery. In the second case, thrombosis occurred on one side and the groin was explored on the erroneous diagnosis of an irreducible inguinal hernia. The authors' interest became aroused following the second case, and within 12 weeks 12 other similar patients were discovered at the antenatal clinics complaining of "lump in the groin".

The authors comment that inguinal herniae are rarely seen in pregnancy, whereas a varicocele of the round ligament appears for the first time early in pregnancy.

No special treatment is required.

Eileen Wilson

155. **Emergency Mitral Valvotomy at Full Term.**

By T. C. J. O'CONNELL and R. MULCAHY. *Brit. med. J.*, **1**, 1191–1192. May 14, 1955. 4 refs.

When mitral valvotomy is indicated in pregnancy, the best time is in the early months. This report shows that operation is still feasible as an emergency procedure at term.

The patient, aged 35, had had no trouble in earlier pregnancies and there was no history of rheumatic fever. She had booked at the hospital's antenatal clinic in this pregnancy but defaulted later and was not seen again

until she was admitted in early labour. At that time it was observed that she was considerably distressed with orthopnoea, cough and cyanosis. There were classical signs of mitral stenosis with slight cardiac enlargement. Her haemoglobin level was only 55 per cent.

She did not respond to medical treatment and 48 hours later she developed signs of impending pulmonary oedema. The labour pains ceased soon after admission.

When she had been treated for 3 days, another unhappy feature was that an area of pulmonary consolidation was not being influenced by antibiotics and it was decided to operate on her heart. The mitral valve was found to be tight and the pulmonary artery large and tense.

After a short labour, a live infant weighing 8 pounds 4 ounces was easily delivered 10 hours post-operatively.

Convalescence was uneventful and she was able to return to the normal active life that she had led before pregnancy.

Doreen Daley

156. **Diabetes and Pregnancy.**

By T. W. ADAMS. *Obstet. Gynec.*, **5**, 160–164. Feb. 1955. 8 refs.

Adams reviews the outcome in 140 pregnancies associated with diabetes occurring between 1941 and 1954 at the Wilcox Memorial Hospital, Portland, Oregon. One hundred and one of these reached the age of viability, and 16 babies were lost. There was a marked reduction in foetal loss in recent years although hormone treatment was not generally used, and the author ascribes this improvement to cooperation between physician and obstetrician. He shows that the optimum time for delivery is the 36th to 38th week, and there is little to choose between vaginal delivery and Caesarean section. If, however, the presenting part is high and the cervix unripe, the latter is the method of choice. The appearance of ossification in the distal femoral epiphysis as shown by intra-uterine radiography has proved useful in determining foetal age.

J. G. Dumoulin

157. **Primary Peritoneal Implantation of an Ovum.**

By W. E. KROUPA and J. E. BLEICHER. *Obstet. Gynec.*, **5**, 165–170. Feb. 1955. 7 refs.

Primary peritoneal implantation of an ovum is rare, there being only 15 reported cases. Diagnosis is frequently missed because repeated vaginal examinations are not usually made during pregnancy. A history of spotting and lower abdominal pain may arouse suspicion although either or both may be absent. Spurious labour near or at term without engagement and progressive dilatation, with the outline of a uterus separate from the abdominal mass, are the most positive indications of abdominal pregnancy. With intra-abdominal bleeding from placental separation the abdomen becomes hard and distended. Signs of shock ensue. A high transverse position of the foetus is seen on X-ray. The foetus usually but not always dies before the sixth month. Lithopaedion or adipocere may follow foetal death.

At laparotomy in the authors' case a 24- to 26-weeks stillborn foetus was delivered. The placenta was situated on a large soft pedunculated fibromyoma on the posterior aspect of the left broad ligament. It was removed with the fibroid.

J. G. Dumoulin

LABOUR

158. **Hazards of Grand Multiparity.**

By H. OXOM. *Obstet. Gynec.*, **5**, 150–156. Feb. 1955. 8 refs.

The grand multipara is described by the author as an obese, overtired, hypertensive woman with poor muscle tone and a tendency toward anaemia. In 63,140 confinements (1926–1952) at the Royal Victoria Hospital, Montreal, there were 1,056 para-7 or more. Of these, 80 per cent were over 35 years old and 25 per cent over 40.

One hundred and fifty had toxaemia and 6 eclampsia. There were 23 cases of abruptio placentae, 20 of placenta praevia, 25 with heart disease and 4 with cervical cancer.

As regards foetal position, transverse lie occurred 24 times (4 were twins), face and brow 3 times and breech 107 times. Forceps deliveries were carried out on 22 occasions, version and extraction 36 times. In 64 patients there was post-partum haemorrhage (over 500 ml.), and in 18 manual removal of the placenta. Ruptured uterus occurred twice. Heart failure occurred 6 times during labour and puerperium, causing 2 deaths. In 26 cases, there was cord prolapse.

The total foetal loss was 135 (12·4 per cent), and the maternal mortality 10 (0·9 per cent) with sepsis and haemorrhage playing leading roles.

The author gives an interesting table comparing the more common and serious complications in the grand multipara with those in women who have produced less than 8 children.

J. G. Dumoulin

159. **The Question of Induction of Labour in Cases of Early Rupture of the Membranes at Term.** (Die Frage der Geburtseinleitung bei verzeitgem Abgang der Fruchtwassers am Termin.)

By J. KAUTSKY. *Gynaecologia, Basel*, **139**, 145–154. Mar. 1955. 5 refs.

Between 1948 and 1953, the author studied the effect of medical induction of labour in all cases with premature rupture of the membranes at term in the Obstetrical Clinic of the Medical Faculty, University of Prague. Attempts to induce labour in such cases often lead to danger of increased operative interference and higher mortality. The best results were obtained where no attempt was made to provoke the onset of labour, but where labour was allowed to begin spontaneously. Induction is not even necessary to avoid a risk of infection. Oxytocin (Pituitrin) and quinine proved more dangerous than Partergin (methylergometrinetartrate).

Josephine Barnes

160. **Present-day Concepts of Manual Removal of the Placenta.**

By W. O. THOMAS, JR. *West. J. Surg. Obstet. Gynec.*, 63, 129–143. Mar. 1955. 30 refs.

Current teaching in America is that manual removal of the placenta is a dangerous procedure carrying a mortality of 0·4–1·8 per cent and a morbidity of 20–25 per cent; the risks of the retained placenta are however considerable and with the advent of antibiotics and blood banks a more daring attitude is developing. The author considers two groups of patients in an endeavour to assess the risks. The first group of 48 cases occurred between 1937–44 (an incidence for the hospital of 0·27 per cent) when only sulphonamides were available; 8 patients became infected but there were no deaths. In the second group between 1950 and 1953 there were 324 cases (an incidence of 1·8 per cent); 9 patients became septic and there were no deaths. Prematurity and operative delivery seem to predispose to the necessity for the operation but the author found that multiparity was not a factor in his series. Retention of the placenta over 1 hour is associated with a considerably increased blood loss and morbidity rate than where the 3rd stage is shorter. Eighteen patients in the second series had uterine packs inserted but, with adequate doses of antibiotics, none became morbid. In the total series of 36,315 deliveries there was 1 placenta accreta, treated by hysterectomy. The author concludes that early removal of the placenta with the use of antibiotics and transfusion does much to improve the morbidity rate and recommends that the third stage should not be allowed to last for more than 15 minutes.

[This is a very good review of the subject.]

D. C. A. Bevis

161. **Repeated Post-partum Hemorrhage.**

By J. R. DORAN, S. A. O'BRIEN and J. H. RANDALL. *Obstet. Gynec.*, 5, 186–192. Feb. 1955. 13 tables. 15 refs.

During the years 1936–1945 there were 12,468 deliveries at the State University of Iowa Hospitals. There were 640 cases of post-partum haemorrhage (600 ml. loss or more). A woman's chance of having a post-partum haemorrhage is 1 in 20, and the incidence of recurrence in a future pregnancy is no greater. So far as parity is concerned, the primiparous patient is more likely to bleed than either the multipara or grand multipara. A woman with a complication of pregnancy is more likely to develop a post-partum haemorrhage than one whose gestation is normal. Primary uterine inertia predisposes to bleeding as does forceps delivery. A prolonged third stage also predisposes to haemorrhage and the authors favour early manual removal of placenta where indicated.

Uterine atony causes 9 out of 10 post-partum haemorrhages, the rest being due to cervical or vaginal bleeding.

In the 640 cases there were 7 deaths (1·1 per cent). Thirty-eight per cent of the cases had a febrile puerperium most commonly due to endometritis. Only 24 per cent were transfused.

J. G. Dumoulin

162. **Pain in Obstetrics.** (Il dolore in ostetricia.)

By M. RIVIERE and L. CHASTRUSSE; R. PIGEAUD and R. GARMIER. *Minerva ginec., Torino*, 7, 46–68. Jan. 31, 1955. 140 refs.

At the Congress of the Latin Mediterranean Society of Obstetrics and Gynaecology held at Turin in 1954 the main theme was Pain. The papers presented have recently been published and the above are worthy of notice, especially as the second is from the University of Lyons where so much work has been done on the relief of pain in the female pelvic organs by Professor Cotte and others.

Labour pain is the only example of a physiological process accompanied by such pain as might be held to act as a discouragement to the conservation of the human race. (On the other hand it is useful in that it warns women of the need to put themselves under conditions where their infants can be safely and securely born; and in the lower animals a similar warning is received and acted upon.) It is possible to get over this paradox by adopting the theory associated with the name of Grantly Dick Read which can be expressed thus: "Childbirth is a natural process and should not be painful. Labour pain is only the result of the false interpretation of an aggressive stimulus which is really painless. Correct the false mental attitude and you abolish the pain." Unfortunately the problem is not quite so simple as that. Whether the pain is real or imagined we must admit it is almost always an accompaniment of labour in greater or lesser degree.

Expulsion pains can reasonably be explained by the extreme compression and stretching of the soft parts during the second stage, and though of great clinical importance are of less interest physiologically.

Dilatation pains are much more difficult to explain. They are only felt at the height of the uterine contractions. The midwife or accoucheur is easily aware with a hand on the fundus of a commencing contraction before the parturient feels it. According to Polaillon's measurements the normal intra-uterine pressure between pains is from 20 to 35 mm. Hg and rises in the contractions of the dilatation stage to from 70 to 100 mm. before falling to its former level. Pain is felt so long as the pressure is about 12 mm. above normal, and if between pains the pressure does not return to normal the woman continues to feel discomfort. This appears to be borne out by the pain felt in the uterus during insufflation tests when the pressure reaches a certain level. Against this, however, it is argued that oxytocics can be given (in attempts to induce labour) which cause very considerable rises in intra-uterine pressure without producing pain so long as they fail in their objective of starting labour. Due perhaps to man's orthostatic posture, the human cervix is a much more powerful structure than that of other animals and it is known to be very richly supplied with sensory nerve terminals, but these react to stretching rather than to other painful stimuli. The cervix can be seized with volsella or cauterized without pain but its dilatation with dilators is acutely painful. The conclusion is that dilatation pains of labour are provoked by strong contractions of a distended uterus trying to force

a sphincter rich in sensory nerves. Some believe that a temporary ischaemia is also a factor.

As for the paths of conduction of dilatation pain, the problem is fairly simple. Operations to interrupt the channels or to anaesthetize them prove that the route is through the presacral and lumbar sympathetic and parasympathetic, and efficient methods of anaesthetizing them can abolish these first stage pains. Pain from the perineum during the expulsive stage travels by the spinal sensory route.

Finally, it is clear that preconceived anxiety and fear greatly increase the perception of pain, and these characteristics are more common among the more sheltered and sensitive classes of women. It is among just such classes that a policy of reassurance and the inculcation of confidence and of an appreciation of the high spiritual role they are playing can give the best results in mental and physical preparation for labour.

W. C. Spackman

OBSTETRIC OPERATIONS

163. **Cesarean Section–Total Hysterectomy.**
By E. H. WEIGLE. *West. J. Surg. Obstet. Gynec.*, **63**, 123–128. Mar. 1955. 16 refs.

The author reports the results of combined Caesarean section–total hysterectomy in 20 patients during the past 4 years. Only 2 of the operations were performed as emergencies, the other cases having uterine pathology [chronic cervicitis figures largely in the list of indications] or required a sterilizing procedure. Spinal anaesthesia was used and there were no operative difficulties. There were no deaths but 1 patient developed a pelvic abscess.

D. C. A. Bevis

MATERNAL MORTALITY

164. **Maternal Mortality in the Pennsylvania Hospital.**
By R. M. MITCHELL. *Obstet. Gynec.*, **5**, 123–136. Feb. 1955. 18 tables.

This is a tabular survey of 150 maternal deaths between 1929 and 1953 occurring in the Philadelphia Lying-in Hospital. It is divided into three 8-yearly periods and demonstrates the great improvements that have taken place over these years. For example, there were 100 deaths in the first period and 17 in the last.

[It is not possible to review adequately this detailed survey which must be studied in the original to be appreciated.] *J. G. Dumoulin*

INFANT

165. **The Paediatrician's Part in the Maternity Services.**
By N. B. CAPON. *Brit. med. J.*, **1**, 803–808. Apr. 2, 1955. 22 refs.

This Lloyd Roberts lecture is a masterly review of the development of interest in the special problems of the newborn infant and makes fascinating reading.

The author's summary gives a better indication of the theme of the lecture than could any abstract and is reproduced in full.

The status of newly born babies has been rising steadily for many years, and this movement was greatly accelerated when pathological studies of stillbirths and neonatal deaths were vigorously undertaken during the first two decades of the present century.

The appointment of paediatricians to the staffs of maternity units has already yielded valuable results and is likely to be even more fruitful in the future.

The loss of infant life by stillbirth and neonatal death is still considerable (27,794 in 1953) and should receive fuller attention, along with the problems of morbidity in the neonatal periods.

The pressure under which maternity units are working at the present time presents dangers so far as the babies are concerned. Questions such as the accommodation and nursing care of the babies need careful study if the incidence of neonatal infection is to be reduced and its spread more effectively controlled.

The proper treatment of the premature baby requires special provision in maternity units, and adequate arrangements for the domiciliary care of those that do not require admission to a ward for the premature.

More should be done to give expectant mothers training in mothercraft, and to advise them in regard to diet, hygiene, preparation for breast-feeding, etc. Paediatricians are well equipped to assist in this service.

In studying the causes of stillbirth and neonatal death it is essential that each case should be considered jointly by obstetrician, pathologist, and paediatrician, bearing in mind that several causes may operate simultaneously or in succession. These causes may be primarily maternal, paternal, placental, or foetal. Conclusions based upon studies made mainly from one angle, whether obstetrical, pathological, or paediatric, are open to the criticism of over-simplification. In each case of stillbirth or neonatal death it is necessary that an agreed aetiological "priority order" should be reached. And if, as is reasonable, the conclusions are to be of value in preventing morbidity as well as mortality in young infants, the studies should not be restricted to the antenatal period and the first week after birth, but should include the whole of the neonatal period.

Doreen Daley

166. **The Large Fetus.**
By A. C. POSNER, S. FRIEDMAN and L. B. POSNER. *Obstet. Gynec.*, **5**, 268–278. Mar. 1955. 13 refs.

This report concerns babies weighing over 9 pounds (4082 g.) born at Harlem Hospital, New York, in 1949–1954. There were 547 (3·4 per cent), 500 of them negro. Large babies would appear to be 2 or 3 times commoner in white than negro patients. Only 0·6 per cent of the babies weighed over 10 pounds in the authors' series. Eighty-seven per cent of the mothers were multiparas, 20 per cent grand multiparas. There were 12 (2·2 per cent) known diabetic mothers in the series. Nine per cent of all mothers delivering infants weighing over 10 pounds were diabetic. It is pointed out that not only

the mother but also the father of a large baby may be prediabetic.

Toxaemias of pregnancy were 3–4 times more frequent among the mothers of large babies.

The Caesarean section rate in the group was 3·7 per cent compared with 2·8 for all babies, and the forceps rate 5·3 per cent. Of the 9 breech deliveries, 3 babies died. Serious foetal birth injuries occurred in 5·5 per cent of babies over 10 pounds and in 0·2 per cent between 9 and 10 pounds. The main maternal complication was post-partum haemorrhage.

J. G. Dumoulin

167. **Fetal Salvage.**

By B. J. HANLEY. *West. J. Surg. Obstet. Gynec.*, **63**, 161–165. Mar. 1955.

The author reviews the results of his own practice between 1947 and 1952; 4,000 consecutive private patients were delivered without maternal mortality but 50 babies died (21 stillborn and 29 neonatal deaths). This mortality was about one-third the rate for the State of California and the author considers that 8 of the babies might have been saved if better judgment or skill had been shown at the time of delivery. He considers that this reduced loss is about the limit to be reached until further discoveries are made in this field of medicine.

D. C. A. Bevis

168. **Exchange Transfusion in Haemolytic Disease of the Newborn.**

By W. WALKER and G. A. NELIGAN. *Brit. med. J.*, **1**, 681–691. Mar. 19, 1955. 4 figs. 31 refs.

Part I—Treatment

These workers at the University of Durham make a more comprehensive survey of the use of exchange transfusion than has been possible in previous papers from that school, for they can now report 272 cases so treated since 1947. All infants were treated within 9 hours of birth and 60 ml. of blood per pound was regarded as the minimum quantity that could be regarded as adequate, 80 ml. per pound being used whenever possible. The indication for this treatment varied at different times as follows:

(1) March, 1947–September, 1949. Any first affected infant clinically affected within 8 hours of birth or a subsequent infant within 24 hours.

(2) October, 1949–August, 1951. This was the period of the national trials and by the rules exchange transfusion was used only if the cord haemoglobin level was 14·8 g. per cent or less. Control cases being used, the number receiving exchange transfusion was reduced to 44 cases during this time.

(3) September, 1951–March, 1954. All babies with anaemia of the above degree were regarded as suitable and also those with a haemoglobin level up to 17·7 g. per cent if the cord bilirubin level was 2·8 mg. per 100 ml. or more. In this period 162 of 264 (61 per cent) affected infants met these criteria. No infant left without transfusion died or developed kernicterus and none needed simple transfusion in the first 3 weeks of life.

The disproportionate risk of kernicterus between mature and premature babies is the basis of the view that on the rare occasions when exchange transfusion needs to be repeated, it will be the small babies who require it and a bilirubin of 25 mg. per 100 ml. has provisionally been taken as the critical level. Only 4 repeat exchange transfusions were done prior to March, 1954 and altogether in that year there were 8 premature and 5 mature infants so treated.

The age at time of transfusion was usually 4–6 hours and decided by convenience as well as by clinical assessment of the baby. This few hours delay may be advantageous if the infant's condition is poor for other reasons than haemolytic disease, though immediate treatment may be called for in grossly anaemic infants.

The volume of blood exchanged was not related to the severity of the disease though occasionally the standard 80 ml. per pound was not quite reached if the baby gave cause for anxiety towards the end of the transfusion. A secondary aim of transfusion was to achieve a final haemoglobin level of 15–17 g. per cent.

In the past 5 years, only 3 out of 245 infants selected for exchange transfusion did not receive an adequate transfusion, 2 from technical failure and 1 *in extremis* which died during transfusion.

In assessing results, the authors stress the difficulties of comparison with other series, for increasing accuracy of diagnosis through the years increases total numbers and indications for treatment vary in different centres. Division into groups indicates the increased risk for the premature baby and the ones born outside centres with full treatment facilities.

Group 1. Twenty-two infants weighing 5½ pounds or less were treated with 6 deaths from haemolytic disease (27 per cent) and 6 other deaths. Three received multiple exchange transfusions.

Group 2. Thirty-seven mature infants born at home or in small hospitals were not all treated within 9 hours of birth. Four died from haemolytic disease (11 per cent) and 3 from other causes.

Group 3. Mature infants born in hospitals with special facilities and selected for treatment on the lines described showed a mortality of 2·6 per cent from haemolytic disease (5 out of 191 cases), 3 others being lost from other causes.

Follow-up results were that 12 per cent of infants needed "topping-up" transfusion because the haemoglobin level had fallen to 8·5 g. per cent. After a year, study of the first 200 cases showed 2 definite and 1 probable case of kernicterus. Later follow-up is being arranged.

Part II—Technique

[A very full account of technical details is given and space only allows mention of a few points in this abstract.]

The umbilical cord was used for transfusion and supernatant plasma was removed from the blood which was usually only a few days old. No account was taken of the sex of the donor except for a retrospective study which showed no evidence of sex difference in the results. Calcium and heparin were not considered necessary. The transfusion set consists of a metal and glass syringe

with Luer-lock fittings to two two-way taps with a large bore, the distal one connecting with a cannula which is inserted into polythene tubing. This catheter is introduced 8–10 cm. and through it the blood is exchanged 10 ml. at a time. On rare occasions when the catheter cannot be satisfactorily introduced through the umbilicus the vein can be exposed through a skin incision 1 to 2 cm. above the cord. Venous pressure is measured by elevating the external part of the catheter and a level below 10 cm. from the abdominal wall is regarded as normal. If the pressure is high, it is advised that 20 ml. should be withdrawn for each 10 ml. injected until the level becomes normal. If the cord haemoglobin level is under 11 g. per cent, a negative balance of 10 ml. for every 10 per cent below this level is recommended. Oxygen therapy should be available for use during the transfusion if necessary.

After-care included encouragement of breast feeding and vitamin K therapy but in the later cases antibiotics were not given as a routine.

Sepsis, air embolism, portal vein thrombosis or perforation of the umbilical vein were not seen in this series. Unwittingly, incompatible blood was given on 2 occasions but in neither case did serious harm result. In about 40 per cent of cases, the infant's condition deteriorates during the transfusion, which normally takes about 75 minutes. Heart failure is most liable to occur in those with a high venous pressure and shock is another risk. A spell in an oxygen box often brings improvement and the transfusion was sometimes temporarily discontinued for resuscitation.

Doreen Daley

169. **Controlled Clinical Trial of Effects of Alevaire Mist on Premature Infants.**

By W. A. SILVERMAN and D. H. ANDERSON. *J. Amer. med. Ass.*, **157**, 1093–1096. Mar. 26, 1955. 4 figs. 7 refs.

It has been suggested that pulmonary complications in premature infants are reduced when they are placed immediately after birth in incubators with atmospheres of 90 to 100 per cent relative humidity. These have been the standard operating conditions at the Babies Hospital, Columbia University, where the authors have now studied the effectiveness of added detergents (Alevaire mist). Two hundred premature infants were divided at random into two groups. One hundred and five infants were treated with Alevaire and 95 were designated as controls treated by the standard operating conditions. Prophylactic antibiotic treatment was the same in both groups. The first 72 hours of life was chosen as the period of clinical trial and death of the infant as the criterion of comparison. The crude death rate within the 72-hour period was not significantly different in the two groups (with Alevaire 22·0 per cent, controls 25·3 per cent). The autopsy findings were essentially the same in the two groups with regard to atelectasis, hyaline membrane, pneumonia, and intracranial haemorrhage.

By a very careful analysis of the different factors in the two groups which could have caused variations the ordinary play of chance was eliminated. Although the group treated by Alevaire mist appeared to lose less initial weight no therapeutic benefit as judged by the death rate and autopsy findings could be credited to the Alevaire. The over-all 28 day mortality rates of the two groups were not significantly different.

D. W. James

GYNAECOLOGY

170. **Endocrine Allergy. The Use of Intradermal Tests in Gynaecology.** (L'allergie endocrinienne. La pratique des intradermo-tests en gynécologie.)

By P. MAGNIER. *Gynéc. prat.*, **6**, 35–53. 1955.

As it records a large number of small series of cases this article is most difficult to abstract. It is concerned with the use of intradermal testing for hormonal allergy in gynaecological practice.

The first part of the paper is devoted to a consideration of allergic manifestations in gynaecology with special reference to premenstrual tension. It is then suggested that in some patients showing such symptoms there is, in the second half of the cycle, a true hyperoestrinaemia which can be demonstrated by vaginal cytology. In other patients with the same symptoms there is no laboratory evidence of excessive oestrogen production. In this last group an intradermal test with water soluble oestrone was positive in 87 per cent as against 17 per cent in the first group. A control group of normal patients gave negative results in 100 per cent.

The author has then progressed to the use of liposoluble preparations of oestradiol, oestrol and oestrone. Oestradiol has been most used as it is obtained in a chemical state of greater purity, a matter of importance in this work.

With this he is able to carry out the test before ovulation and finds that it becomes positive at about the time of ovulation. He does not claim this as a test to indicate the occurrence of ovulation, but merely as indicating a time when ovulation is probable. He suggests it may be of some use in defining the period of fertility. Its main use is, however, in the detection of states of allergy to oestradiol.

The article includes some experiences with intradermal progesterone and testosterone. Neither of these procedures appears to have given results of any value. Testosterone tests on pregnant women have been used in attempts, so far unavailing, to define the sex of the foetus *in utero*.

The author concludes that the procedure of intradermal testing with hormones is too recent for any definite conclusions to be drawn. Although several other publications are cited, there are, unfortunately, no references.

Geoffrey Dixon

171. **First Degree Amenorrhoea.** (Amenorrea de primer grado.)

By R. G. GIARDINI. *Obstet. Ginec. Lat.-amer.*, **12**, 529–531. Oct. 1954. 9 refs.

The author uses the term First Degree Amenorrhoea to imply that a deficiency of progesterone is present, and is responsible for various menstrual irregularities. The

oestrogen production may be normal or slightly diminished. Two grades of progesterone deficiency are described: (1) partial, which causes oligomenorrhoea or polymenorrhoea, but never amenorrhoea; (2) complete, in which case the behaviour of the Graafian follicle determines the menstrual irregularity.

Diagnosis of progesterone deficiency is made by three methods: (1) colpotomy, to observe the condition of the ovary, and the presence of atretic follicles; (2) examination of the cervical mucus for crystallization, which can be produced if no corpus luteum has been formed; (3) clinico-therapeutic effect of giving 25–50 mg. of progesterone intramuscularly, which causes metrorrhagia (provided the endometrium is in a state of proliferation). This effect is produced by interrupting oestrogen metabolism, whereby oestrone is converted into oestriol, which always causes bleeding in 4–5 days. If bleeding does not occur, it is advised that a repeated dose should not be given within 15 days in case spontaneous cure is occurring.

In a survey of 77 cases, the author found that, in 24 patients on whom all three methods of investigation had been used, the colposcopy and progesterone tests agreed in each case, but the cervical mucus crystallization test disagreed in 2.

In 53 of the 77 cases, which had been investigated at an earlier date, the cervical mucus test had not been employed as it was not then a routine procedure.

In the majority of these cases, the period of amenorrhoea varied between 30 and 50 days. The author found that, in 87 per cent of patients, metrorrhagia occurred between the 4th and 5th days after the intramuscular injection of progesterone.

John F. Foulkes

172. **Diagnostic and Therapeutic Errors in Certain Dermatoses of the Vulva.**

By E. P. SCHOCH, JR., and C. H. MCCUISTION. *J. Amer. med. Ass.*, **157**, 1102–1106. Mar. 26, 1955. 8 figs. 12 refs.

The confusion that exists in regard to terminology, diagnosis, and treatment of certain dermatoses of the vulva is partly due to lack of co-operative study by gynaecologists, dermatologists, urologists, and psychiatrists. The authors attempt to clarify the position with special regard to those that they do not consider to be precancerous. The conditions under consideration are kraurosis, lichen sclerosus, circumscribed scleroderma, lichen planus, senile atrophy, neurodermatitis, and leukoplakia. Tabulated comparisons of the histological and clinical features are given.

The term "primary sclerosing atrophy" is suggested to include kraurosis and lichen sclerosus which are fundamentally the same. Secondary infections and pruritus account for the various phases of the vulvitis which often complicate this condition. Lichen planus may involve the vulva alone, but the histological picture is typical. There are many aetiological factors in pruritus vulvae, but when the term is used by the dermatologist it usually refers to idiopathic pruritus. When accompanied by lichenification it is more accurately described as neurodermatitis. Senile atrophy cannot be explained by oestrogen deficiency alone for oestrogen therapy will not reverse the changes. The cause of scleroderma is unknown.

Leukoplakia may arise in the normal skin of the vulva, on simple senile atrophy, or on the primary sclerosing atrophy. It is the only condition regarded as precancerous and should be treated by vulvectomy or electrodesiccation if only small lesions are present. The benign dermatoses are treated by the usual palliative methods and vulvectomy as a prophylactic against cancer is not recommended in the uncomplicated primary sclerosing atrophies.

D. W. James

173. **Psychosomatic Aspects of Sterility.** (Aspectos psicosomáticos de la esterilidad.)

By W. H. PERLOFF. *Obstet. Ginec. Lat.-amer.*, **13**, 1–4. Jan./Feb. 1955.

Although anxiety and tension in husband or wife may not appear to have a physical influence in causing sterility, the author presents various aspects and clinical manifestations of deep seated neuroses, which he has found on investigation.

Impotence in the husband, which is only present when his wife is not menstruating, is a typical example. Similarly some cases of low spermatozoa count have been found to improve when given a course of psychotherapy; one such case in the author's series increased the count by 100 per cent with this treatment, and his wife conceived.

Intense longing for pregnancy in the female often masks a profound subconscious desire to avoid it, which may be manifested in many different ways, such as spasm of the Fallopian tubes, vaginismus, failure to ovulate and apparent stupidity during investigation—the patient makes varied excuses for not recording basal temperatures, etc.

The author maintains that, if the doctor makes very tactful enquiries in a leisurely manner in these cases, very often he finds a sub-conscious fear of some kind or other. In such cases, assurance that they are healthy and normal is all that is necessary to relax the patients' anxiety. In other cases, with a deep seated fear of pregnancy, the author states that to inform the patient that he or she is sterile is sometimes most effective, although somewhat embarrassing to explain when the patient returns pregnant at a later date.

In conclusion, the writer expresses the belief that in some cases, where the would-be parents are intensely neurotic, sterility is a fortunate state, but nevertheless he asserts that it is one's obligation to cure sterility wherever possible.

John F. Foulkes

174. **Physiology of the Testis.**

By E. T. ENGLE. *J. Urol.*, **73**, 544–546. Mar. 1955.

Our knowledge of the physiology of the testis has not progressed much in recent years. The following points appear to be accepted:

(1) Testosterone is manufactured by the interstitial cells.

(2) Oestrogens can be extracted from the testis of bulls and stallions.

(3) Oestradiol can be extracted from human testis.

(4) Sertoli cells in the dog produce oestrogens.

(5) Large quantities of lipid material in the Sertoli cells are a degenerative sign.

(6) Spermatogonia and Sertoli cells in normal young men are high in mucopolysaccharides. When testicular fibrosis is present these substances are much reduced.

There are two obvious gaps in our knowledge: (1) The role of the steroids in spermatogenesis. (2) The action of the pituitary gland in relation to the testis. In the case of pituitary gonadotrophins the preparations are protein in nature and are too impure and of low potency. It is possible that our knowledge of steroid metabolism may be increased as a result of the present day treatment of inoperable breast cancer.

J. H. Carver

175. **Tromexan Haematoma in a Penicillin Sensitive Patient.** (Tromexanblutung in Penicillinexanthem.)

By H. STAHL. *Gynaecologia, Basel*, **139**, 184–189. Mar. 1955. 4 figs. 5 refs.

A case is reported where penicillin sensitivity gave rise to two large eruptions on the thighs. Later administration of "Tromexan" caused the appearance of two haematomas. These were associated with a superficial necrosis of the skin. A warning is given of the danger of using anticoagulants in the presence of drug sensitivity.

Josephine Barnes

176. **Pelvic Tuberculosis: A Report on 19 Cases.**

By A. KOUYOUMDJIAN. *Brit. med. J.*, **1**, 829–831. Apr. 2, 1955. 3 tables. 10 refs.

Data of 19 cases of tuberculosis of the female genital tract investigated at the American University Hospitals, Beirut, are presented. They occurred amongst 2,492 admissions, an incidence of 0·8 per cent, in the 7 years after 1946.

The symptoms in order of frequency were:

Dull lower abdominal pain, sterility, low-grade fever, watery vaginal discharge, abdominal swelling due to ascites and menstrual disturbances which might be irregularity, amenorrhoea or menorrhagia. Only 15 per cent had dysmenorrhoea.

Examination revealed masses in the fornices in 6 cases and thickening in a similar number. Nothing abnormal was detected in 3 cases, fibroids were diagnosed in a further 3 cases and cervical carcinoma was suspected in a case where the biopsy revealed tuberculosis.

Thirteen of the 19 cases had a chest X-ray and in 7 of these there was evidence of past or present infection. There was leucocytosis in 8, lymphocytosis in 5 and anaemia in 8 cases.

Histological studies showed the disease in all the material from the 10 cases where the tubes were examined, in 11 out of 13 curettings and 2 of 5 cervices. Ovaries examined from 10 cases showed lesions in only two.

Mention is made of curettage, culture of menstrual blood and its inoculation into guinea-pigs and hysterosalpingography [but these diagnostic aids do not seem to have been assessed by the author].

Doreen Daley

177. **Streptomycin Therapy for Asymptomatic Endometrial Tuberculosis.**

By M. SUZUKI. *Obstet. Gynec.*, **5**, 142–149. Feb. 1955. 15 refs.

From Hiroshima comes this report on the use of streptomycin in 20 patients with asymptomatic endometrial tuberculosis. Daily dosage of 1 g. intramuscularly was given for 40 days. The complete course was given to 15 patients, and treatment was stopped in 4 cases because of toxic reactions. One case refused a complete course of injections. All continued work during the treatment. The effect of the therapy was evaluated in 18 cases.

Of the 15 patients who had adnexal thickening, 11 showed evidence of its decrease or disappearance. Follow-up endometrial biopsies showed the disappearance of tuberculous lesions. During the 2-year follow-up, 2 patients became pregnant, one aborting and the other having an ectopic gestation.

Hysterosalpingograms were done before and after treatment in 13 cases, showing a disappearance or reduction of uterine irregularity. In 4 whose tubes were non-patent before the treatment there was some patency after. In the majority with occluded tubes, the block was in the isthmic portion.

In the endometrial biopsies tuberculous foci decreased and usually disappeared after 30 days. Six patients showed a relapse 6 months to 2 years after therapy.

J. G. Dumoulin

NEW GROWTHS OF THE REPRODUCTIVE ORGANS

178. **Paget's Disease of the Vulva: Report of a Case.**

By P. L. FEDERICI. *Obstet. Gynec.*, **5**, 171-174. Feb. 1955. 3 figs. 4 refs.

Paget's Disease of the Vulva: Review; Report of Two Cases.

By J. D. WOODRUFF. *Obstet. Gynec.*, **5**, 175–185. Feb. 1955. 8 figs. 36 refs.

These two articles add another 3 cases of Paget's disease of the vulva to the total of 21 which have been reported in the literature (which is reviewed). This intra-epithelial lesion may progress to invasive carcinoma. Woodruff considers the origin of the disease to be from the clear cells which are probably involved in the production of pigment and from the cells of the epidermis involved in the production of the apocrine glands. Wide excision is the treatment of choice.

J. G. Dumoulin

179. **Metastatic Pulmonary Chorionepithelioma with Recovery in Two Cases.**

By J. F. NOLAN, E. M. COOK and W. E. DALLKE. *West. J. Surg. Obstet. Gynec.*, **63**, 101–106. Mar. 1955. 8 figs. 8 refs.

The treatment of 2 cases of chorionepithelioma is reported. In the first case the removal of a benign hydatidiform mole was followed 3 months later by sudden vaginal bleeding and the radiological appearance of two nodules in the lungs which appeared to be metastases. Total hysterectomy with bilateral salpingo-oöphorectomy was performed, the specimen showing avascular chorionic villi invading the cornu of the uterus almost to the serosa. The larger nodule (in the right lung) was irradiated using Cobalt 60, 5,500 r being given over 66 days, This nodule disappeared within 4 months but the nodule in the left lung disappeared without treatment in 3 months. The patient has remained well for 2 years. The second case had an abortion followed 4 months later by the appearance of a nodule in the anterior vaginal fornix and a positive Friedman test. Biopsy showed a chorionepithelioma and a total hysterectomy was performed, the appendages, parametrium, upper vagina and pelvic lymph nodes being also removed. The specimen showed a choriocarcinoma involving the myometrium, left tube, endocervix and vagina. Cobalt 60 irradiation was begun 10 days later, 1,000 r being given to the parametrium over 23 days; at the end of this time a mass 4 cm. in diameter was found in the parametrium; 1,000 r was delivered to this in 7 days. At the same time multiple small nodules were found in both lung bases and the Friedman test was positive. Nitrogen mustard 6 mg. i.v. was given for 3 days and radiotherapy resumed, 1,000 r being given to the pelvic mass over 15 days and 1,000 r given to each lower lung field over 8 days. The serum Friedman became negative in 3 months and the nodules in the lungs and pelvis had disappeared within 3 weeks. The patient has remained well for 2 years. The first case is considered now to have had a benign tumour and the behaviour and nature of the nodules in the lungs remain unexplained. The second case is thought to have been a true choriocarcinoma but the relative merits of radiation and nitrogen mustard cannot be evaluated but it is thought that this method may offer something in the difficult case.

[Technical details of the radiotherapy are given in the original paper.]

D. C. A. Bevis

180. **Sarcoma and Sarcoma-Like Proliferations of the Endometrial Stroma. 2. Carcinosarcoma.**

By R. E. Symmonds and M. B. Dockerty. *Surg. Gynec. Obstet.*, **100**, 322–328. Mar. 1955. 3 figs. 15 refs.

The authors consider that the term "carcinosarcoma" should be limited to those single neoplasms exhibiting at the time of examination an intimate mixture of carcinomatous and sarcomatous tissue but lacking heterotopic or dysontogenic elements as present in mesodermal mixed tumours.

At the Mayo Clinic from 1910 to 1952, 20 patients were encountered with tumours which presented histologically a combination of sarcomatous and carcinomatous elements. Nine were true carcinosarcomas and the article consists of a review of these cases.

The average age of the 9 patients was 54·1 years. Eight had passed the menopause, but menstruation of 5 of these had ceased following a menopausal dose of radium or roentgen rays. This unusual incidence of a history of irradiation therapy associated with carcinosarcoma has been noted previously by other workers. Eight of the 9 patients had noticed post-menopausal bleeding and the symptoms did not differ appreciably from those associated with other uterine malignant lesions.

In each case the tumour consisted of a discrete polypoid lesion with a narrow to broad base. The polypoid sarcomatous elements were almost everywhere quite delineated but the carcinomatous portions, when visible grossly, tended to involve the endometrial surface more diffusely. In 3 of the 9 cases there was no clinical evidence of extension of the tumour and gross examination of the surgical specimens failed to reveal any infiltration of the myometrium. In the remaining 6 specimens there were grossly apparent deep penetration of the myometrium and extension to the contiguous structures.

Microscopically the bulk of each tumour was found to consist of sarcomatous tissue. The carcinomatous component of the mixture consisted of adenocarcinoma in 7 and adenoacanthoma in 2 cases. Although 5 of the 9 patients had received menopausal doses of irradiation years before their tumours were discovered, it was not possible to adduce microscopic evidence for a cause and effect relationship. The necrosis and infection present frequently in these growths seemed best explained on the basis of their tendency to prolapse through the cervical os and undergo infarction as a result.

All the cases were treated by total abdominal hysterectomy and bilateral salpingo-oöphorectomy. Six patients received post-operative roentgen therapy. Four patients were living without evidence of recurrence for periods varying from 1·5 to 9·5 years following operation. In 3 of these the lesions were limited to the endometrium and in the fourth the tumour had penetrated the myometrium almost to the serosa and in addition had infiltrated to the left broad ligament.

The value of irradiation could not be ascertained from the very limited number of cases.

John P. Erskine

181. **Environmental Factors in Cervical Cancer.**

By E. L. Wynder. *Brit. med. J.*, **1**, 743–747. Mar. 26, 1955. 5 figs. 12 refs.

The author, from the Sloan-Kettering Institute, New York, has studied the role of environmental factors in cervical cancer. Patients were interviewed in nine different hospitals in the United States, and controls were selected with other pelvic disorders. The analyses were based entirely on epidermoid cancer. Indian patients were selected at the Tata Memorial Hospital, Bombay, a total of 892 cancer patients, and 1,826 controls were included in the study. In the group of patients from America, the incidence in Jewish women was very low. In the group from India, the relative rate was very high in Hindus, high in Christians and Negroes, but low in Parsees and Moslems.

There was no statistical evidence that pregnancy rate

was of importance as a factor in production of cervical cancer. The abstinence period practised by orthodox Jews did not seem to account for the low incidence in Jewish women.

It was a striking fact, however, that the cervical cancer group married significantly earlier than the control group. The Indian data showed a significantly earlier onset of first coitus among Hindus and Moslems as compared with Indian Christians and Parsees.

The factor of circumcision in the partner was investigated. In all groups the incidence of cancer was much higher in women exposed to uncircumcised male partners. As it was not possible to investigate directly the female hygiene in the partners of the patients studied, males from the hospital population were examined, and divided into different economic, racial and religious groups. The data showed that those male groups have the highest degree of poor penile hygiene whose females also have the highest rates of cervical cancer.

The practice of circumcision in Moslems may counteract the effect of early marriage, and account for the low incidence of cervical cancer.

The authors suggest that universal circumcision might significantly reduce the incidence of cervical cancer.

Eileen Wilson

182: **Prophylaxis of Carcinoma of the Cervix. Diathermy Coagulation of Cervicitis.** (A propos de la prophylaxie pratique du cancer du col. La diathermo-coagulation des cervicites.)

By J. E. MARCEL and A. PYE. *Gynéc. prat.*, **6**, 55–59. 1955. 14 refs.

The authors believe that, until more is known of the aetiology of carcinoma, prevention must lie in the eradication of conditions thought to favour the appearance of the disease. The eradication of chronic cervicitis by diathermy is, they hold, a practical step in this direction and should be more widely practised.

One of the authors has also used diathermy coagulation for several years in the treatment of carcinoma *in situ*, and feels that it is the treatment of choice in that condition.

Geoffrey Dixon

183. **Smears in the Detection of Preclinical Carcinoma of the Uterine Cervix; Further Studies with Emphasis on the Significance of the Negative "Repeats".**

By D. C. DARLIN, L. M. RANDALL, E. H. SOULE and M. B. DOCKERTY. *Surg. Gynec. Obstet.*, **100**, 463–467. Apr. 1955. 4 figs. 8 refs.

The authors describe the practical programme which they have formulated at the Mayo Clinic for the detection of preclinical cervical carcinoma. Cervical scrapings are obtained with the Ayre spatula or cotton applicator sticks from the portio vaginalis and endocervix of each new patient. Smears are prepared and examined by a trained technician who marks suspicious or malignant cells. The marked slides are then analyzed by a pathologist trained in cytology. In all but the negative cases tissue from the squamo-columnar junctional zone is obtained by punch biopsy or by conization.

In the statistics presented, only those cases in which the gynaecologists' clinical diagnosis was that of a benign lesion or a normal cervix are included. To the end of 1953, 30,310 such cases were screened. The incidence of detection of preclinical carcinomas was consistent and averaged 0·89 per cent. Of the 270 malignant lesions discovered, 267 were squamous cell carcinomas of the cervix. Two were adenocarcinomas of the endocervix and only 1 was an endometrial cancer.

The average age of the 243 patients who had carcinoma *in situ* in this series was 42·1 years, whereas that for the 24 patients who had preclinical infiltrating carcinoma, was 49·7 years. On the assumption that the average carcinoma *in situ* should be at the mid-point in its slow evolution when it is discovered, it is suggested that the actual duration of carcinoma *in situ* from the time that it is diagnosable until it infiltrates may be upward of 15 years. Utilizing this data it is calculated that a "pickup" rate of 0·89 per cent is not only reasonable but to be expected.

Repeat smears in women, who had had a previous negative smear at least 3 months and averaging about 1 year previously, were done in 3,025 instances. Preclinical carcinoma was detected in 5 instances (0·17 per cent). The fact that a marked decrease (from 0·89 to 0·17 per cent) in the pickup rate occurred in the repeat smear group is adduced as important evidence that the lesions discovered were in fact significant.

John P. Erskine

184. **Carcinoma-In-Situ of the Uterine Cervix.**

By D. G. MORTON, L. J. ZELDIS and A. MONK. *West. J. Surg. Obstet. Gynec.*, **63**, 185–191. Apr. 1955. 9 figs.

The authors, at the University of California, review 22 cases of early carcinoma occurring over 7 years. Twelve cases were diagnosed by vaginal smears and in 8 of these there were no symptoms or suspicious clinical findings (1,813 patients were examined by vaginal smears). To make sure of the diagnosis multiple sections from multiple blocks of tissue must be examined and it is recommended that a cone be removed from the cervix at least 2 cm. in diameter at the external os and extending 1·5 cm. up the cervical canal. The criteria for diagnosis are:

(1) Failure of the squamous mucosa to differentiate from basal cells.

(2) Pleomorphism and anaplasia of the cells.

(3) Abnormal mitotic activity.

(4) Confinement by the basement membrane of surface mucosa and cells.

These criteria are discussed fully and the use of histochemical methods considered; the periodic acid-Schiff reagent is of doubtful value but staining for the mucopolysaccharide of the basement membrane is sometimes of use. Involvement of the endocervical glands by cancer cells is regarded as evidence of invasive carcinoma.

The material was finally classified into 4 groups: carcinoma *in situ* without gland involvement (3 cases); carcinoma *in situ* with gland involvement (3 cases); cases with questionable involvement of the stroma or lymphatics (3 cases); cases with definite though

minimal invasion (13 cases). Treatment depends on the accurate diagnosis; in true carcinoma *in situ* almost any form of treatment should prove satisfactory, even cauterization. In fact, total hysterectomy has usually been employed, the ovaries being left if the patient is young. The finding of endocervical gland involvement or nests of cancer cells has been taken to indicate invasion and the patients treated by radical hysterectomy or full irradiation, it being considered that it is dangerous to compromise. The only exception to these methods is in pregnancy when the epithelial changes are difficult to interpret; the cervix is carefully rechecked in the puerperium and treatment based on the findings.

The authors conclude that the diagnosis is made far too often and as a result treatment is incomplete in many cases.

[This is a very good review of the subject.]

D. C. A. Bevis

185. **Diagnosis and Treatment of Endometriosis.**

By J. P. PRATT. *West. J. Surg. Obstet. Gynec.*, **63**, 177–180. Apr. 1955.

The symptoms of endometriosis vary with the site of the lesion but the majority of cases are symptomless. If the lesion is found in the uterus, hysterectomy is the treatment of choice but expectant treatment may be tried in a young woman as pregnancy is not impossible. No treatment is indicated for small lesions found incidently elsewhere as there is no evidence that they give further trouble later. Hormonal therapy with oestrogens or androgens is useful for temporary relief and to confirm the diagnosis. Radiotherapy is unsatisfactory unless a castrating dose be given. Excision of the more extensive lesions must be attempted but management is highly individualized as the activity of the lesions depends on ovarian function.

D. C. A. Bevis

186. **Infiltration of the Parametrium as a Clinical Sign of Endometriosis.** (Un signe clinique de l'endométriose: l'infiltration du paramètre.)

By P. FUNCK-BRENTANO, H. ROBERT and J. CURTZ. *Gynéc. Obstét.*, **53**, 535–540. 1954. 2 figs.

At the Gynaecological Clinic of the Broca Hospital the peritoneal form of pelvic endometriosis was shown to be of very frequent occurrence in 45 cases collected between October, 1950 and January, 1954. Nine cases were localized to the utero-sacral ligaments. It was possible in 6 of these 9 cases to suspect this trouble by careful gynaecological examination which revealed infiltration of the parametrium.

These 6 cases are then reported in detail. They concern young women coming for advice generally because of progressive dysmenorrhoea or sterility. The infiltration of the parametrium expressed itself in a retraction of the vaginal cul de sac—a loss of suppleness, diminution in depth or depressibility. The vaginal examination revealed a tenderness above all when the patient was examined about the time of the periods.

On rectal examination one can feel the lateral wall of the rectum like a hard core due to the infiltration of the subperitoneal cellular tissue at the level of the enlarged and tender utero-sacral ligaments.

D. Maxwell

187. **Stilbestrol-Induced Hyperhormonal Amenorrhea for the Treatment of Pelvic Endometriosis.**

By A. L. HASKINS and R. B. WOOLF. *Obstet. Gynec.*, **5**, 113–122. Feb. 1955. 6 figs. 2 refs.

The authors report on the use of large doses of stilboestrol in the treatment of pelvic endometriosis in 15 cases. The method was suggested by Karnaky (*Sth. med. J.*, 1948, **41**, 1109). The dose used started with 1 mg. and was gradually increased to a daily dose of 100 mg., continued for an average of 3 months, and then gradually decreased. The symptomatic response included amenorrhoea and was similar to the response observed in the disease to pregnancy. About 2 days after the last dose all patients had a heavy but never alarming withdrawal bleeding. Remission of symptoms of endometriosis was immediate and gratifying. Nausea and vomiting occurred in most cases in the second week of therapy and rarely exceeded 10 days. Enlargement of the breasts, pigmentation of the skin and a profuse white mucoid discharge usually occurred. Weight gain of 2–4 pounds was noted but no evidence of oedema.

No real change in the size of the endometriotic lesions was found although they became softer and less tender. Biopsy revealed hyperplasia of the endometrium in the lesions.

The patients were treated for an average of 6 months but were symptomless for an average of 20 months. There were 3 pregnancies following treatment. Vaginal spotting of blood occurred frequently after the daily dose of 100 mg. stilboestrol was reached, but no serious bleeding. The authors claim that the symptomatic relief obtained was impressive and the treatment was not harmful.

J. G. Dumoulin

188. **Ureteral Obstruction from Endometriosis.**

By R. K. RATLIFF and W. B. CRENSHAW. *Surg. Gynec. Obstet.*, **100**, 414–418. Apr. 1955. 6 figs. 6 refs.

The authors review the literature regarding this rare phenomenon and add 3 cases of unilateral ureteral obstruction secondary to compression from pelvic endometriosis without bladder involvement.

The first case had a long history of menorrhagia and dysmenorrhoea and later developed dysuria and frequency of micturition. Intravenous pyelograms revealed right hydronephrosis and hydroureter. Hysterectomy and removal of the ovaries was performed but no attempt was made to free the right ureter. Five years later the patient is symptom-free and her pyelograms are normal.

Cases 2 and 3 had long histories of flank and back pain associated with the menses, and in both the left kidney was not visualized on intravenous pyelography. In Case 2 a small mass of endometriosis was found overlying the left ureter at the pelvic brim and was removed. This was followed by X-ray castration but follow-up pyelograms 5 years later showed persistent left hydronephrosis.

Five years after total hysterectomy and bilateral salpingo-oöphorectomy in Case 3 the patient is asymptomatic and her pyelograms are normal.

In discussing the diagnosis it is stressed that:

(1) Pyelographically the obstruction is always seen in the lowest third of the ureter.

(2) There is almost always concurrent pelvic endometriosis.

(3) Although not always present there frequently is cyclical pain, either in the renal or pelvic areas.

(4) Haematuria occurs if there is invasion of the ureteral lumen.

Treatment by castration is recommended especially when there is a chance of salvaging the kidney.

The authors conclude that, while ureteral obstruction from endometriosis without bladder involvement is rare, undoubtedly many cases are overlooked and they have commenced a study by pyelography of a large series of patients with endometriosis.

John P. Erskine

OPERATIONS

189. **Culdoscopy in Pelvic Diseases of Uncertain Aetiology.** (La culdoscopie en las algias pelvicas de etiologie imprecise.)

By J. GALVEZ. *Rev. españ. Obstet. Ginec.*, **14**, 32–34. Jan./Feb. 1955.

The author points out the value of culdoscopy, which enables diagnosis to be made by vision, rather than by blind "touch". He quotes Thompson (*Geburtsh. Frauenheilk.*, 1954, **14**, 925) who, in a statistical follow-up of 5,000 culdoscopies, found that there were few complications. There were slight temperatures in 21, which subsided rapidly after treatment with antibiotics. There were also 5 rectal lesions which cured themselves with no ill effect.

The author used the method in 19 cases. The indications were as follows:

(*a*) To clear up doubts after an apparently normal vaginal examination.

(*b*) Difficulty in making a satisfactory vaginal examination, because of fat, or resistance in the abdominal wall.

(*c*) Because a lump in the region of the adnexa had been found, and in order to decide whether it was an old inflammatory process or a functional disturbance.

(*d*) When a diagnosis of "adnexitis" had been made by other gynaecologists and the diagnosis seemed doubtful.

(*e*) If endometriosis was suspected.

The technique which the author uses is as follows. Firstly he gives a narcotic (Escofedal) half an hour before. No local anaesthesia is necessary. Then he makes a tentative puncture with a needle which is connected to a syringe full of air. The air can often be heard to rush freely into the peritoneal cavity when the needle is withdrawn. If the peritoneal cavity is not penetrated by the needle, the author does not persist with the culdoscopy. He mentions the importance of drawing the posterior lip of the cervix forwards, to put the utero-sacral ligaments on the stretch in order to make the pouch of Douglas wider and more obvious.

Results. In 18 cases out of 19 he was able to carry out a completely satisfactory examination. In 9 cases the internal genitals appeared perfectly normal. In 3 cases there was a persistent small follicle the size of a nut, which had been felt bimanually. In 6 other cases there was residual adnexitis, and in 5 of these no abnormality had been felt bimanually.

The author comments that culdoscopy is a sound method of clarifying the diagnosis, and of decreasing the number of exploratory laparotomies.

[The author mentions the use of no specific apparatus for culdoscopy, other than a needle, trocar or bistoury. It is not clear whether he refers to "naked eye culdoscopy"—or to instrumental culdoscopy. From personal experience of innumerable colpotomies, I would add "? ectopic" to the list of indications, assuming, that is, that it is to "naked eye culdoscopy" he refers.]

D. G. Wilson Clyne

190. **Gynaecography.** (La gynécographie (Technique-indications).)

By G. ROUX, G. MARCHAL and J. CANDON. *Gynéc. Obstét.*, **53**, 545–550. 1954. 3 figs.

The authors have carried out a critical study of the value of multiple contrast media, in particular gases, in gynaecological diagnosis.

Several workers in the past have studied insufflation of the pelvic visceral cavities. Françillon-Lobre combined hystero-salpingography with rectal insufflation and instillation of an opaque fluid into the bladder. Keller used a barium medium in order to outline an ovarian tumour.

Bertrant, Villeneuve and Baillot employed the injections of intraperitoneal lipiodol after puncture of the pouch of Douglas.

Kjellberg in 1942 published his work on hystero-salpingo-pelvigraphy, but this method, although unquestionably interesting, had notable drawbacks, in particular the disadvantage of rarely demonstrating the ovary itself but merely the ovarian fossa.

By gynaecography is meant a study of the internal genitalia of the female after insufflation of gas into the peritoneal cavity.

In 1919 a paper was published by Ribadeau-Dumas, Mallet and de Laulerie concerning the radiological examination of the abdominal viscera after injection of oxygen into the peritoneal cavity.

In 1921 a further paper by Coliez was published on pneumoperitoneum in gynaecology and simultaneously in America Orndorf and Peterson published an article on the same subject.

Finally in 1926 Stein perfected the technique combining hystero-salpingography and pneumoperitoneum.

Technique

(1) *Preparation.* No anaesthetic and no premedication are necessary. An enema is advisable, and the bladder should be empty.

(2) *Production of pneumoperitoneum.* The writers used exclusively the trans-parietal abdominal route. In the dorsal position, with the head unraised and using a

lumbar puncture needle paracentesis is carried out at the classical point for ascites. Oxygen is preferred as the gas. 600 c.cm. a minute are injected and the pressure carefully watched with a manometer. As soon as 400 c.cm. have passed in, the liver dullness usually disappears. An average of 1,500 to 1,800 c.cm. is used.

(3) *X-ray exposures.* The patient is then turned on her front to lie on the Potter-Bucky diaphragm. The table is inclined to an angle of 35° so that the head of the patient lies lower than her feet. Three exposures are made centring on the midpoint of the intergluteal fold.

(4) *Exsufflation.* This is usually unnecessary.

(5) *Hysterography if combined with this gynaecography* allows visualization of the whole of the internal genitals.

The writers conclude that gynaecography can only be a supplementary examination, but, in certain cases, "with no risk to the patient", it can give a certain diagnosis.

Gynaecography must be reserved primarily for studying lesions of the adnexa, just as hysterography is primarily for studying the uterus. *D. Maxwell*

191. **Failures in Sterilization.**

By G. N. Rotton. *West. J. Surg. Obstet. Gynec.*, **63**, 146–149. Mar. 1955. 12 refs.

The author reports 5 cases of failure of tubal ligation. The method used was cornual resection, the tube being crushed at the cornu and 1 inch distally and, after ligation with catgut, the intervening portion excised. In no case was there a demonstrable failure in technique and in 2 cases subjected to laparotomy (for other reasons) no evidence of recanalization of the tube could be discovered. In another 2 cases recanalization had occurred in the mesosalpinx. The fifth patient had a hysterosalpingogram performed and the tubes appeared to be blocked. The author concludes that proliferation of the tubal mucosa (endosalpingiosis) may lead to continuity of the genital tract being restored and advises that resection be carried out at a distance from the cornua.

D. C. A. Bevis

192. **Conservation of Ovaries.**

By J. W. Dowsett. *West. J. Surg. Obstet. Gynec.*, **63**, 156–158. Mar. 1955.

Between 1944 and 1954, 907 bilateral oöphorectomies were performed at the Emanuel Hospital, Portland, and 165 (18 per cent) of these showed no pathology. The author pleads for a more conservative attitude as the tendency for radical surgery is becoming more marked in recent years. He points out that carcinoma of the ovary is rare over the age of 50 and believes that ovaries function for many years after the cessation of the menses; he concludes that prophylactic oöphorectomy should not be performed. *D. C. A. Bevis*

193. **Anterior Rectal Wall Advancement.**

By W. F. Mengert and S. A. Fish. *Obstet. Gynec.*, **5**, 262–267. Mar. 1955. 6 figs.

In 1902, Noble described an operation for complete perineal laceration which consisted of splitting the rectovaginal septum, dissecting the lower end of the rectum from the vagina and drawing the anterior wall of the rectum down through and external to the anus. The authors find the operation simple and useful in the repair of old complete perineal lacerations and rectovaginal fistulas. They obtained a good result in 22 out of 23 cases of old tear. There was 1 death due to reactivation of a latent amoebic colitis. In 9 cases of rectovaginal fistula operated on results were uniformly satisfactory.

J. G. Dumoulin

194. **Vaginal Hysterectomy for Uterine Prolapse. Report of 52 Cases Treated by Modified Spaulding-Richardson Technique.**

By W. H. Mast. *Surg. Gynec. Obstet.*, **100**, 315–321. Mar. 1955. 5 figs. 11 refs.

The author states that the most widely accepted treatment in America for uterine prolapse is vaginal hysterectomy. The mortality rate is low and early post-operative complications are less than with any other procedure. However, shortening of the vagina leads to dyspareunia in 5–10 per cent of cases and the recurrence rate of vaginal vault prolapse is between 2·8 and 35 per cent. As a result there has been renewed interest in the Spaulding-Richardson technique. This composite procedure consists essentially of cervical amputation, removal of the corpus at any desired level, and utilization of the remaining isthmic portion of the uterus for interposition.

The operation as carried out by the author is described in some detail and is clearly illustrated. This differs from the usual technique in that the corpus is removed before the cervix is amputated and the severed ovarian and round ligaments are secured deeply in the coned-out uterine segment rather than to its sides. The importance of pre-operative exclusion of uterine carcinoma by vaginal and cervical smears, and by curettage and cervical biopsy, is stressed. In addition to malignancy a considerable number of contra-indications to the operations are listed.

The data of 52 patients operated on from 1946 to 1953 are presented. There were no deaths, post-operative complications were not frequent and there has been no case of recurrence of prolapse.

John P. Erskine

195. **Utero-vaginal Repairs by the Perineo-Vaginal Approach (Dellapiane's Technique).** (Plastic utéro-vaginale par voie périnéo-vaginale selon la technique de Dellapiane.)

By P. N. Siliquini and G. Pinoli. *Gynéc. prat.*, **6**, 7–33. 1955. 31 figs. 10 refs.

This article is a plea for what is called conservative treatment of uterovaginal prolapse by vaginal repair. The advantage of the type of operation described is stressed as being the preservation of function of the genital apparatus. It is also pointed out that, when it is necessary to remove a diseased uterus at the time of a prolapse repair, the hysterectomy is simply an extension of the operation and that the first concern of the operator

must still be perfect reconstruction of the pelvic supporting structures.

The authors believe that the cause of failure to achieve a good result is failure to obliterate the potential hernial orifices. Attention is drawn in particular to hernia of the pouch of Douglas.

Dellapiane's operation is derived from the technique described by Pestalozza in 1902, a technique which the Manchester operation is said to resemble closely. The main difference between the operation described and the Manchester repair as practised in the United Kingdom is that the posterior dissection is the first step in the operation. This is made through a large transverse perineal incision which is then extended upwards as a ⊥ shaped incision into the vagina. The dissection is continued until the pouch of Douglas is opened and any hernial sac dealt with. The anterior repair is then made in the usual fashion and includes amputation of the cervix. Finally the posterior repair is completed. The modification necessary if vaginal hysterectomy is to be combined is also dealt with at some length.

[Most of the views presented in this article are in complete agreement with current teaching in this country but most gynaecological surgeons will probably not be convinced that the operation described has anything to commend it over the Manchester repair. Unfortunately, no series of cases is presented. The article is profusely illustrated with excellent photographs of the operative technique and most of the steps are also shown in helpful simple line diagrams.]

Geoffrey Dixon

UROLOGY

196. **The Pathology and Clinical Features of Hyperplasia of the Mucosa of the Female Urethra.** (Zur Pathologie und Klinik der hyperplastischen Schleimhautbildungen der weiblichen Harnröhre.)

By K. H. Bruntsch. *Gynaecologia, Basel*, **139**, 164–183. Mar. 1955. 15 figs. 55 refs.

This is a detailed study of 86 cases of mucosal hyperplasia of the female urethra. These are divided into 11 cases of urethral caruncle, 72 polypi and 3 papillomata. Special consideration is given to the differential diagnosis from carcinoma; certain diagnosis can only be made on histological examination.

Josephine Barnes

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Vol. LXII AUGUST 1955 No. 4

CONTENTS

PLACENTA PRAEVIA. A Review of 200 Cases .. 497
F. G. Grant, M.B., M.R.C.O.G.
THE CONSERVATIVE MANAGEMENT OF THE SEVERE TOXAEMIC PATIENT .. 504
A. P. Barry, M.D., M.A.O., F.R.C.O.G., and M. B. Quane, M.B., M.A.O., M.R.C.O.G.
THE PROBLEM OF THE TREATMENT OF PEPTIC ASPIRATION PNEUMONIA FOLLOWING OBSTETRIC ANAESTHESIA (MENDELSON'S SYNDROME) .. 509
W. Hausmann, M.D., M.R.C.P., and R. L. Lunt, M.B., Ch.B., M.R.C.O.G.
STUDIES IN PLACENTAL ACTION DURING PROLONGED AND DYSFUNCTIONAL LABOURS USING RADIOACTIVE SODIUM 513
Trevor Johnson, M.B., B.S., M.R.C.O.G., F.F.A.R.C.S., and C. G. Clayton, M.Sc.
THE EFFECT OF THE HYDROGENATED ERGOTOXINE-GROUP ALKALOIDS ON THE INTACT HUMAN UTERUS .. 523
William J. Garrett, M.B., B.S., and Mostyn P. Embrey, M.D., B.Sc., F.R.C.S.E., M.R.C.O.G.
VESICO-VAGINAL FISTULAE. A Report on the Vaginal Repair of 160 Cases .. 530
Denis W. P. Lavery
A CASE OF PHYSOPYOMETRA .. 540
A. H. C. Walker, M.B., M.R.C.O.G., and D. Pearson, M.B., D.M.R.T.
A STUDY OF THE HISTOCHEMISTRY OF THE HUMAN FOETAL OVARY .. 542
F. Hamilton Leckie, M.C., T.D., L.R.C.P., M.R.C.O.G.
FULL-TIME PREGNANCY AFTER PROVED ENDOMETRIAL TUBERCULOSIS .. 548
Jean L. Hallum, B.Sc., M.D., M.R.C.O.G., D.C.H., and Harold E. Thomas, M.D., M.R.C.P.
PLACENTA ACCRETA ASSOCIATED WITH PLACENTA PRAEVIA .. 551
D. W. James, M.D., M.R.C.O.G., and K. A. Misch, L.R.C.P. & S.E., D.C.P.
ADVANCED EXTRA-UTERINE PREGNANCY. Fifty-two Cases .. 555
G. P. Charlewood, F.R.C.S., F.R.C.O.G., and A. Culiner, M.D., F.A.C.S., M.R.C.O.G.
AN UNUSUAL CASE OF SECONDARY ABDOMINAL PREGNANCY .. 560
W. D. Giffen, M.B., F.R.C.S.E., M.R.C.O.G.
ORAL AND VULVAL ULCERATION WITH INFLAMMATION IN THE EYE .. 562
C. J. Dewhurst, M.B., F.R.C.S.(Ed.), M.R.C.O.G.
ENDOMETRIAL SARCOMA COMPLICATING CYSTIC HYPERPLASIA. With Remarks on "Carcino-sarcoma" .. 567
P. E. Hughesdon, M.B., and D. Pells Cocks, M.D., M.R.C.O.G.
THE APPEARANCE OF LIPOID IN THE GENITAL TRACT OF THE IMMATURE FEMALE GUINEA-PIG .. 572
R. S. Snell, M.B., M.R.C.S., and T. Nicol, M.D., D.Sc., F.R.C.S., F.R.C.S.E., F.R.S.E.
THE FUNCTIONAL ACTIVITY OF THE GENITAL TRACT IN POST-MENOPAUSAL ENDOMETRIAL CARCINOMA .. 574
John M. McBride, B.Sc., M.D., M.R.C.O.G., F.R.F.P.S.G.
INTRA-UTERINE PASTES FOR THERAPEUTIC ABORTION .. 585
Geoffrey F. Williams, M.B., M.R.C.O.G., E. A. Danino, M.D., M.R.C.P., and Vyvyan J. Davies, M.D., F.R.C.S.E.
TREATMENT OF ECLAMPSIA WITH BROMETHOL .. 589
Dr. P. Madhavan, B.A., M.D., and Dr. K. Bhasker Rao, M.D.
FOETAL RENAL HYPOPLASIA AND THE ORIGIN OF AMNIOTIC FLUID .. 592
G. H. Green, B.A., B.Sc., M.B., M.R.C.O.G.
DYSTOCIA CAUSED BY CONGENITAL HYDRONEPHROSIS AND BLADDER DISTENSION .. 597
W. J. S. Still, M.B., Ch.B.
VAGINAL PLUG FOR PROCIDENTIA IN ELDERLY WOMEN .. 599
McKim McCullagh, D.S.O., M.C., M.B., F.R.C.O.G.
FRACTURE OF THE SPINE IN PREGNANCY .. 600
A. E. R. Buckle, M.B., M.R.C.O.G.
A CASE OF SPONDYLOLISTHESIS IN PREGNANCY .. 603
David Byron Brown, M.B., Ch.B.
MONO-AMNIOTIC MULTIPLE PREGNANCY. A Report of Five New Cases .. 605
John K. Wilson, M.B., M.R.C.O.G.
MONO-AMNIOTIC TWINS WITH ONE BLIGHTED. Case Report .. 610
D. B. Whitehouse, M.A., M.D., M.R.C.O.G.
A SIMPLE APPARATUS FOR RESUSCITATION OF THE NEWBORN .. 612
N. L. Wulfsohn, M.B., B.Ch.(Wits.)
SOME ASPECTS OF BREECH DELIVERY .. 614
R. G. Law, M.D., M.R.C.O.G.
AN UNUSUAL CASE OF BLOOD DISEASE IN PREGNANCY .. 622
Elsie M. Sibthorpe, M.D., M.R.C.O.G.
VARIATIONS IN PALMAR SWEATING DURING PREGNANCY .. 626
P. C. B. MacKinnon, M.B., Ch.B., and I. L. MacKinnon, M.B., Ch.B.
INTRA-UTERINE MEASUREMENT OF PRESSURE DURING LABOUR. Sources of Error .. 629
A. Ingelman-Sundberg and L. Lindgren
A PRIMARY BROW PRESENTATION .. 636
H. E. Mcnamara, M.D., D.Obst.R.C.O.G.
PREGNANCY AFTER EXTENSIVE MYOMECTOMY .. 638
G. Gordon Lennon, Ch.M., F.R.C.O.G., M.M.S.A.
ACUTE MONOCYTIC LEUKAEMIA IN PREGNANCY .. 640
Wallace Barr, B.Sc., M.B., M.R.C.O.G.
ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS .. 644
REPORTS OF SOCIETIES .. 646
BOOK REVIEWS .. 653
REVIEW OF CURRENT LITERATURE .. 655
NOTICES .. 672

ND
RE
No. 4

497
504
509
513
523
530
540
542
548
551
555
560
562
567
572
574
585
589
592
597
599
600
603
605
610
612
614
622
626
629
636
638
640
644
646
653
655
672